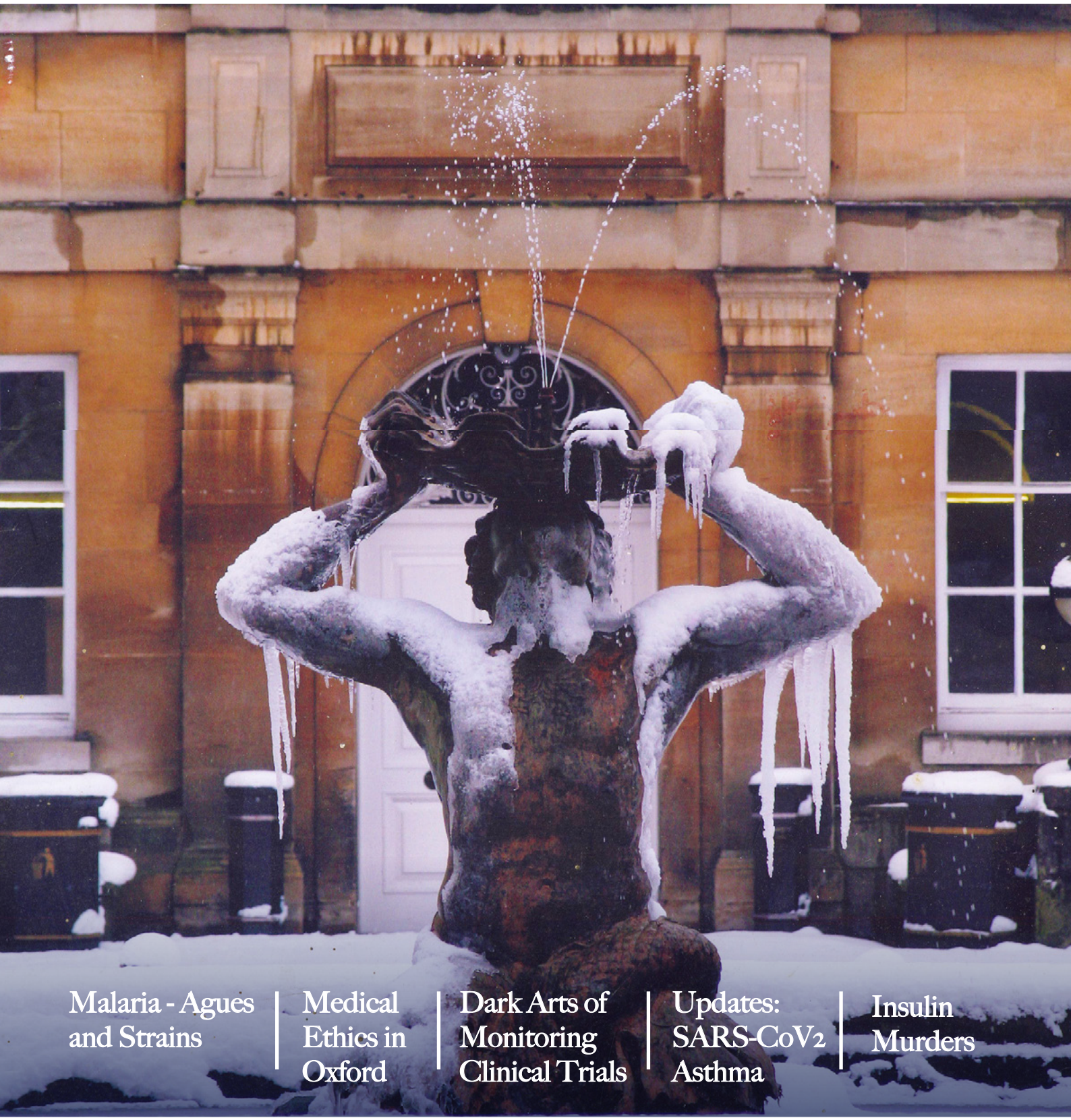
Oxford Medicine

THE MAGAZINE OF THE OXFORD MEDICAL ALUMNI

Oxford Medical Alumni

UNIVERSITY OF OXFORD

Autumn/Winter 2021



Malaria - Agues and Strains | Medical Ethics in Oxford | Dark Arts of Monitoring Clinical Trials | Updates: SARS-CoV2 Asthma | Insulin Murders

Pictured: Frozen Radcliffe Triton Fountain © Robin Frith

Oxford Medical Alumni Update

Oxford Medical Alumni (OMA) promotes good fellowship amongst Oxford Medical Sciences alumni, supports regular meetings in Oxford, and elsewhere, for continued learning, exchange of ideas, networking and socialising.

REUNIONS

Decade reunions are planned for alumni every year. In 2022, reunions will be scheduled for alumni who qualified in 1972, 1982, 1992, 2002 and 2012, with catch-up reunions also planned for 1970 and 1971. Details will be sent by email and will be advertised here: **www.medsci.ox.ac.uk/get-involved/alumni/events-and-reunions/oxford-medical-school-reunions**

CAREER ADVICE FOR JUNIOR DOCTORS

OMA recognises the challenges facing young doctors, some of whom are seeking inspiration and advice on their future careers. We feel OMA could play a role in facilitating informal relationships around career advice. If you feel you can help, please contact Dr Will Seligman (seligmanw@gmail.com). We are particularly looking for consultants, GPs and senior trainees who qualified between 1990 and 2010 and are up to date with training programs and consultant recruitment.

RECONNECTING WITH FRIENDS AND COLLEAGUES

If you would like to reconnect with friends and colleagues you have lost contact with over the years, please email us at oma@medsci.ox.ac.uk and we will try our best to help.

MEETING MINDS, 06 - 08 APRIL 2022

The University of Oxford creates the virtual opportunity for alumni around the world to come together and experience an array of exciting and innovative talks, with speakers sharing their experiences and expertise across a diverse range of topics. The lecture series will be accessible online: **www.alumni.ox.ac.uk/meeting-minds.** You will need to create a My Oxford Online account in order to see them (they're behind a firewall) accessed via our website: **www.alumni.ox.ac.uk/my-oxford/my-oxford-online**

OXFORD MEDICAL AUSTRALIA MEETING

The next event is planned at Peppers Noosa Resort in Queensland. Details to be confirmed.

RECOLLECTING OXFORD MEDICINE

Enjoy the first 50 interviews in the Recollecting Oxford Medicine series. Inspired by Dr Peggy Frith, this is a unique collection of oral history about medicine at Oxford from the 1940s onwards through face-to-face interviews. Dr Derek Hockaday's hard work and skilful interviewing over the last 14 years, has produced this special collection: **www.podcasts.ox.ac.uk/series/recollecting-oxford-medicine-oral-histories**

OXFORD MEDICAL LECTURE CLUB

The Oxford Medical Lecture Club invites distinguished, entertaining and interesting speakers to talk about their specialty and the latest developments in clinical and scientific research. The meetings are now held at St Hugh's College on the last Monday of each month.

Future speakers:

Monday 31 January 2022: 'Renal Anemia – has EPO had its day?' Professor Chris Winearls (1972 Keble College), Associate Professor of Medicine at the University of Oxford and Emeritus Fellow and former Senior Research Fellow in Clinical Medicine at Jesus College, Oxford.

Monday 28 February 2022 'Brain Fever. How vaccines prevent meningitis and other killer diseases.' Professor Richard Moxon (1968 Keble College), Emeritus Professor of Paediatrics and a Professorial Fellow of Jesus College, Oxford.

If you are interested to receive notifications of the meetings, please contact oma@medsci.ox.ac.uk. Details of previous lectures can be found here: **www.medsci.ox.ac.uk/get-involved/alumni/events-and-reunions/oxford-medical-lecture-club**

CONTRIBUTIONS TO *OXFORD MEDICINE*

We welcome your contributions to future editions of *Oxford Medicine* - clinical, scientific, creative, reflective, humorous, prose or poetry. We would like to represent the full spectrum of alumni young and old, near and far.

OMA ADVISORY BOARD (OMAAB) MEMBERS

Dr Lyn Williamson (President), Dr Roger Bodley (Honorary Treasurer), Dr Zoi Aexopoulou, Professor Sir John Bell, Sir Michael Dixon, Ms Christine Fairchild, Dr Shing (Tom) Law, Dr Laurence Leaver, Dr Tim Littlewood, Dr David McCartney, Professor John Morris, Ms Bella Pratt, Professor Gavin Screaton, Dr William Seligman, Dr Eric Sidebottom, Professor John Stein, Dr Catherine Swales, Dr Robert Wilkins, Dr Kevin Windebank, and Miss Carolina Valensise.

OMA THANKS

We owe a huge debt of gratitude to Ms Christine Fairchild for steering OMA through the last couple of years of staff changes and pandemic restrictions. We bid a fond farewell to Ms Rebecca Ward, who for the past year has worked as interim Alumni Relations Manager. We thank her for her hard work and dedication and wish her well in her new post. We warmly welcome Ms Bella Pratt as our new Alumni Relations Manager and look forward to working with her.

CONTACT PREFERENCES

Please let us know if any personal details have changed or go to the OMA website to update yourself.

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Designed by Jess Aumonier

President's Piece

Dr Lyn Williamson
OMA President

Esprit de Corps

With contributions spanning eight decades of alumni, we hope every reader will feel the warm glow of belonging. Our recent OMLC speaker, Simon Wessely, emphasised that being part of a team or family, is a crucial factor in resilience and coping with difficulties and disasters. And there are plenty of these on the horizon....

Our student 'Climate Crisis = Health Crisis' campaign reminds me of Tony Hope as an earnest medical student campaigning for the study of medical ethics. His lone voice was joined by others, and gradually led to Oxford becoming an internationally renowned centre for the study of ethics and humanities.

But this all took decades to develop, and we don't have decades. However, we do have hope that the urgency and cooperation applied to the Covid pandemic are transferred to other communicable diseases and the climate crisis. Meanwhile, remember that no single snowflake believes it is responsible for the avalanche.

Noble Deeds in a Minor Key

One of my pleasures is meeting alumni at reunions and hearing their stories. Developing our One World theme, we feature contrasting accounts from home and abroad – Oxford, Wolverhampton, Thailand, Uganda, Malawi and China - often condensing decades of work into single nuanced sentences. They are modestly told, entertaining and inspiring.

Sound the Trumpet

Our stellar line-up of contributors offers us a rich and varied array of masterpieces – reviews, reflections, recollections, and updates. Witty, wise, thought-provoking, and occasionally indiscrete. Each is a gem.

Creativity abounds: Tingewick returns live in January, and the next Radcliffe orchestra performance is in March. We start and finish with photos from alumni that reflect the beauty and fragility of our planet.

Season's Greetings and wishing you all good health.

FEATURES

CLINICAL UPDATES

COMMENT AND CONTROVERSIES

MEMORIES AND REFLECTIONS

OMA ABROAD

NEWS AND REVIEWS

MEDICAL SCHOOL NEWS

CREATIVE OMA

Malaria - Agues and Strains

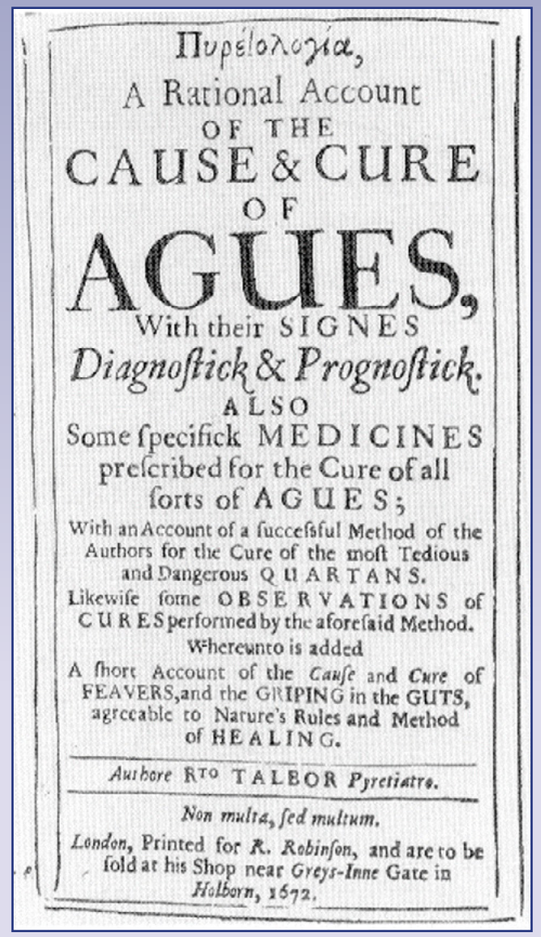
Professor Sir Nick White
Professor of Tropical Medicine, Mahidol and Oxford Universities

We think of malaria today as a tropical disease but, until the early twentieth century, the infection ranged as far north as the Arctic Circle and was prevalent throughout Europe and the Eastern half of North America. The British defeat at the decisive battle of Yorktown in the American War of Independence has been blamed (by some!) on the debilitating effects of malaria on the British and German troops. Oxford has a long history of research on malaria and its treatment. Over 350 years ago, Thomas Sydenham (a former Fellow of All Souls) and Thomas Willis (Christchurch and founding member of the Royal Society, Sedleian Professor of Natural Philosophy at Oxford, and bitter rival of Sydenham), both wrote extensively about fevers, and their experience of treatment of *agues* with the newly introduced Jesuit's bark. The bark of the Cinchona tree contains the antimalarial alkaloids quinine, quinidine (the diastereomer of quinine), cinchonine and cinchonidine.

Before he took up the Regius Professorship in Oxford, William Osler was very familiar with malaria in Baltimore (where he may have been the first to institute a routine blood test-the malaria blood smear-in all febrile patients).

In 1902, the second Nobel Prize in Physiology or Medicine was awarded to Ronald Ross for his discovery that "dapple winged" (anopheline) mosquitoes transmitted malaria. Nearly two decades later, in Oxford, London, Epsom and Aldershot, Ross led large studies of antimalarial treatment in soldiers returning from the First World War. In 1924, the first synthetic antimalarial (plasmoquine) was discovered by scientists working for Bayer in Germany. Then followed mepacrine (1932) and chloroquine (1934), but most of the world still relied on quinine -and by then 90 per cent of the world's quinine supply came from the island of Java (where the Dutch had planted the high yielding *Cinchona ledgeriana*). During the Second World War, military authorities, knowing that malaria often killed more soldiers than bullets during wartime, and that a Japanese expansion in the Pacific would endanger the quinine supply, instituted a desperate search for synthetic alternatives. In the United States, chloroquine was rediscovered and, in the UK, a new type of antimalarial (proguanil; Paludrine®) was discovered by chemists at ICI. Proguanil was evaluated initially in Liverpool and in Oxford. After the War, following the success in eliminating malaria from Europe and North America, the newly formed World Health Organisation (WHO) embarked on an ambitious attempt to eradicate all malaria from the world. It is often said that this was successful in eliminating malariologists but failed to eliminate malaria. In the aftermath of this failure, malaria went off the agenda and by the 1970s, was returning with a vengeance across the tropical world.

In 1979, supported by David Weatherall from the Nuffield Department of Medicine and the Wellcome Trust, David and Mary Warrell left Oxford for Thailand to set up a small research collaboration in the Faculty of Tropical Medicine of



Πυρέτολογία,
A Rational Account
OF THE
CAUSE & CURE
OF
AGUES,
With their SIGNES
Diagnostick & Prognostick.
ALSO
Some ſpecifick MEDICINES
preſcribed for the Cure of all
ſorts of AGUES;
With an Account of a ſucceſsful Method of the Authors for the Cure of the moſt Tedious and Dangerous QUARTANS.
Likewiſe ſome OBSERVATIONS of CURES performed by the aforeſaid Method.
Whereunto is added
A ſhort Account of the *Cauſe* and *Cure* of FEAVERS, and the GRIPING in the GUTS, agreeable to Nature's Rules and Method of HEALING.
Authore RTO TALBOR *Pyretiatro.*
Non multa, ſed multum.
London, Printed for *R. Robinſon*, and are to be ſold at his Shop near *Greys-Inne* Gate in *Holborn*, 1672.

Although Sydenham and Willis may have differed, all the physicians were united in their disdain (? jealousy) of (Sir) Richard Talbor, an apothecary, who won fame and fortune, and the recognition of both Charles II and Louis XV. Using the "English remedy", his own special concoction of the Cinchona bark, Talbor cured the tertian fevers of both Charles II and the dauphin, the last living son of Louis XIV.

Mahidol University in Bangkok. I joined a year later having had some training in the MRC Department of Clinical Pharmacology under David Grahame-Smith. Initially we studied snake bite, rabies and, in Eastern Thailand - severe malaria. For reasons which still remain a mystery, antimalarial drug resistance usually starts first somewhere near the Thailand-Cambodia border. By the 1980s, strains of *Plasmodium falciparum* (the main cause of malaria deaths) resistant to chloroquine and several other antimalarials were widespread in Southeast Asia and we had been forced to return to quinine for the treatment of falciparum malaria. But there was confusion about the dose. The Cinchona dose regimens had not changed much since those recommended by the Jesuits in the "Schedula Romana" 350 years previously, but they had been challenged by recent research in the Vietnam War. It was now recommended

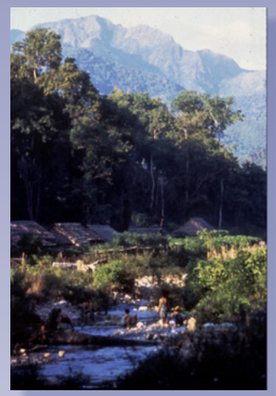
Pelletier and Caventou discovered the structure of quinine in 1820 (they also later discovered the structures of caffeine and strychnine). This bronze statue stood in the centre of Paris (arrondissment 5, Val-de-Grâce) from 1900 until 1942, when it was melted down during the occupation.

that the treatment of severe malaria (mortality about 20 per cent) should be with a quinine dose as little as one sixth of that previously used. By studying patients with severe malaria and characterizing plasma concentration profiles using simple ("old-fashioned") drug measurement (benzene -extraction spectrofluorimetry), we could show that this dose reduction was incorrect and potentially lethal, and to propose instead a higher loading dose regimen. This proved safe and effective. After some initial reluctance, the loading dose treatment regimen was eventually endorsed by WHO. Meanwhile in Africa, where most deaths from malaria occur, the parasite strains were more drug sensitive and chloroquine was working well, although there were increasing

The geographic distribution of malaria a century ago.

concerns about the cardiovascular toxicity of parenteral administration. Then, in 1984, the WHO abruptly announced that parenteral chloroquine should no longer be used. At that time, malaria was killing about a million children each year in Africa, and there was no alternative to chloroquine in most of the continent! In pharmacokinetic studies in Zambia and The Gambia, we showed that simple adjustments to the dose regimen were all that was needed to make parenteral chloroquine safe. Unfortunately, chloroquine resistant parasite strains soon swept across Africa and, as in Asia, quinine (at the new correct doses!) had to be reintroduced for severe malaria.

In Thailand, we were studying a new antimalarial drug (mefloquine) which had been developed by the US Army during the Vietnam War. In 1984, forced by the increasing failure of the other antimalarial drugs, Thailand was the first country to deploy mefloquine. Unfortunately, the initially recommended dose was too low (a recurring problem with antimalarial drugs). This probably contributed to the rapid emergence and spread of mefloquine resistant strains of *P. falciparum*. Although we could show that higher doses of mefloquine were more effective and reasonably well tolerated, resistance rapidly worsened. By the early 1990s, we were facing potentially untreatable malaria. Our salvation was a Chinese herb (qinghao; *Artemesia annua*). We had visited China first in the early 1980s to learn about Qinghaosu (*artemisinin*). Remarkable claims had been made for the herbal medicine, which seemed to be too good to be true. We were offered the Chinese drugs for testing by Professor Li Giao Quo (the key clinician in the Chinese project 523 discovery programme), but we were dissuaded by WHO. They were worried about the purity of the Chinese medicines and promised that they would soon provide us with a quality product for testing. The politics behind the scenes was complex and convoluted, and worthy of a le Carré novel, but suffice to say that WHO never did provide the drugs. In the end, the Southeast Asian countries voted with their feet and started to import (and in the case of Vietnam) cultivate and produce artemisinins. We were able to obtain the Chinese drugs (sometimes via mules over the China-Burma border, sometimes via suitcases of drugs from markets in Ho Chi Minh City) and study them. The Chinese claims proved correct – the artemisinins were more rapidly acting antimalarials than anything we had ever seen, and they were very well tolerated. Indeed, they were so well tolerated and effective that fakes (falsified medicines) soon appeared. We took the Chinese drugs to The Gambia in West Africa in 1989 and then, in a large programme (the Shoklo Malaria Research Unit; SMRU) led by Francois Nosten, began to develop and evaluate artemisinin combination therapies (ACTs) on the Northwestern border of Thailand. Malaria was then the main disease affecting the large refugee population, largely comprising the Karen ethnic minority, who had been displaced by ongoing conflict in Myanmar. Each year we treated thousands of patients in refugee camps, and later in border clinics, but we needed effective antimalarial medicines. Mefloquine alone was now failing badly. Another antimalarial developed by the US army called halofantrine proved better than mefloquine, and it had no nasty central nervous system side effects, but we found it caused potentially lethal ventricular arrythmias (the marked ECG QT prolongation had somehow been missed in development). Fortunately, the ACTs proved to be the best antimalarial treatments ever



The camps for "displaced persons" on the once malarious Northwestern border of Thailand where the first studies of artemisinin combination treatments took place.

The severe malaria ward in the Hospital for Tropical Diseases Ho Chi Minh City, Vietnam, in 1991. This is where the severe malaria randomized controlled trials started.

-although there was reluctance by International agencies to accept the Chinese medicines outside Asia. In 1995, we began to test a new ACT from China called artemether-lumefantrine. This was also introduced initially at a dose that was too low but, after we found the correct dose, its use expanded. Today, it is the most widely used antimalarial drug in the world. In 2005, the ACTs were finally recommended by WHO as first line treatments for falciparum malaria everywhere in the world. They have contributed substantially to the global decline in malaria mortality. Some five hundred million ACT treatments are now given each year.

Meanwhile, in Vietnam from the beginning of the 1990s, the newly formed unit in the Hospital for Tropical Diseases, Ho Chi Minh City, began to test whether the artemisinins could replace quinine in the treatment of severe malaria. These detailed clinical investigations led us on to conduct multinational randomised trials in Asia and then Africa. These RCTs showed that artesunate reduced the mortality of severe malaria by about one third. It was also better tolerated, easier to give, and less expensive. Artesunate is now the treatment of choice for severe malaria everywhere (including Oxford!).

Throughout the early 2000s, there had been rumours of treatment failures following artemisinin treatments. At first these could be attributed to fake drugs but by 2007, it was clear that artemisinin resistant strains of *P. falciparum* had really emerged in the Pailin area of Western Cambodia (Pailin also had the dubious distinction of being the Khmer Rouge headquarters in the 1980s). Unfortunately, resistance soon emerged in other parts of the Greater Mekong subregion and, with modern molecular genetic techniques, we followed the evolution and spread of successful individual malaria parasite lineages over four countries. Artemisinin resistance led to ACT partner drug resistance. Strains of *P. falciparum* resistant to artemisinins and their ACT partner drugs pose a major threat to malaria control and to the renewed global commitment to eliminate malaria. The latest piece of bad news is the independent emergence of artemisinin resistant strains in East Africa. So, what can be done? New drugs are still years away from general deployment. We do now have a reasonable malaria vaccine, which provides short term protection, but availability is limited. So, we are hoping to persuade the rather conservative malaria community that malaria (like TB and HIV) should be treated with three drugs, not two. These triple ACTs (TACTs) which use existing drugs work well but, given how slowly international agencies have responded to previous malaria challenges, I am not confident these will be adopted in time. But let us end on a high note – pioneered by and then implemented by SMRU - falciparum malaria has been all but eliminated on the Northwestern border of Thailand. We used to enrol thousands of patients a year in our clinical trials. Now we cannot find a single case!

Slow traffic on the road to the camps

Development of Medical Ethics in Oxford

Professor Tony Hope
(1970 New College) Professor of Medical Ethics, University of Oxford; Emeritus Fellow St Cross College; Honorary Fellow New College and Honorary Consultant Psychiatrist.

The University of Oxford has a byzantine structure. That is a strength. It may be difficult to start new ventures but, if pursued with sufficient determination, it is nigh on impossible for anyone to stop them. Like the mushrooms in my lawn.

The University of Oxford has two internationally renowned research groups working in medical ethics: *The Ethox Centre* and *The Uehiro Centre*. The former is in the Medical Sciences Division; the latter in the Philosophy Faculty. The two centres work closely together. In collaboration they have created a third grouping: *The Wellcome Centre for Ethics and Humanities*. No other British university, and few across the world, have such breadth and depth in medical ethics.

How this came to pass is a meandering, and perhaps a uniquely Oxford, story. It involves clinical medical students, the NHS, the Medical School, faculties and colleges, our man in Japan, and crime fiction.

If one person can be credited as the originator of medical ethics in Oxford that person is Jonathan Glover. He was tutor in philosophy at New College in the 1970s, one of the leading moral philosophers of his generation, and a medical ethicist before there was such a subject.

I first met Glover when I came to New College in 1970 to read physiology and philosophy (PPP). Glover's tutorials were Socratic dialogues, with a glass of sherry. He listened to my essays without interruption and then, through questioning, led me to see the absurdities of my arguments. On one occasion he summed up: 'So, Tony, you believe that the morally right thing to do is to kill everyone in the world, painlessly.'

Global Health Bioethics Network Summer School in Oxford. The participants are from 15 different countries. © Dinnah Rippon

In the late 1970s, in the Department of Psychiatry, Bill Fulford, a young lecturer, was working towards a DPhil. Nothing unusual about that. What was unusual was that the DPhil was in linguistic philosophy. At the same time, issues in medical ethics were being discussed in medical schools. Ranaan Gillon, editor of the *Journal of Medical Ethics*, was encouraging students and doctors to write about ethical issues in clinical practice. Ted Shotter had founded the *London Medical Group*, a student-led society, which organised seminars in ethics across several London medical schools. In Oxford, Mary Ryan, Murray Longmore and I started the *Oxford Medical Forum*. Muir Gray, then a young public health doctor, hearing of this initiative, enthusiastically helped get the *Forum* off the ground. He gave his own money to pay speakers' travel expenses and set up an Advisory Committee that met once a term. The Committee was chaired by Sir Richard Doll. It included several senior professors. It included Derek Parfit – a megastar of Western philosophy – and also economist Amartya Sen, who went on to win the Nobel Prize. In how many universities would clinical students be given such support?

> *"..a uniquely Oxford story. It involves clinical medical students, the NHS, the medical school, faculties & colleges, our man in Japan, and crime fiction'*

In the late 1980s, Oxford clinical students organised their own questionnaire to find out what they wanted covered in the medical curriculum. Their report landed on the desk of Sir David Weatherall, then Nuffield Professor of Medicine. In that report the students asked for seminars in ethics and communication skills. Entirely by chance, in the same week, a proposal for seminars for clinical students in ethics and communication skills also landed on Weatherall's desk. That proposal was written by Fulford and me. Weatherall saw the opportunity to develop the teaching beyond our proposal. He suggested that we write an application to the Leverhulme Trust to develop a course in these areas, and to produce materials of value to medical schools throughout the country. The project was called *The Oxford Practice Skills Project*. The applicants were Weatherall himself, and Caroline Miles.

Caroline Miles was chairman of Oxfordshire Health Authority. She refused to be called *the Chair*: 'I am not a piece of furniture'. She had extensive experience at a high level in both public and private sectors. Described as 'one of Nature's Head Girls' she was feared by many. Behind the forbidding façade, however, there was a kind, loyal and approachable person. On one occasion she joined my wife and me and our young daughters for the teddy-bear weekend at Cogges Farm (near Witney) and brought her own much loved, and much worn, teddy-bear to the picnic.

In 1990, the Leverhulme Trust funded an administrative secretary - Anne Yates - and me, for four years, with Fulford and Miles as unpaid advisors. Our first meetings were held at a table at The League of Friends in the John Radcliffe Hospital. After much opposition, the Hospital and University agreed to create an office in what was then the wide, long corridor on level three.

Caroline Miles suggested that the Project needed an Advisory Panel. Her networking skills were second to none and she brought together an extraordinary mix of people. Her stroke of genius was to invite the Chairman of the General Medical Council (GMC) Education Committee. Two years later, in 1993, that Committee published its seminal document on medical education: *Tomorrow's Doctors*. This document outlined the medical curriculum that the GMC required all medical schools in the UK to follow. For the first time, both ethics and communication skills were included as core parts of the curriculum, no doubt influenced by the chairman's experience on the Oxford Practice Skills Project Advisory Panel.

The teaching of ethics and communication skills in Oxford medical school began in 1991. There was no curriculum time given to these subjects. Every seminar had to be negotiated with those few friendly consultants who would allow the students, attached to their firms, time to attend. Whilst Fulford and I had some expertise in ethics, we had very little in teaching communication skills. Luckily, Oxford had one of the country's leaders in medical communication, the general practitioner Theo Schofield. Schofield was co-author of *The Consultation*, the book that popularised the importance of establishing a patient's 'ideas, concerns and expectations'. The book was better known as 'Pendleton et al.' and Schofield often referred to himself as 'et al.' The book also established 'the Pendleton rules' for giving feedback: first concentrate on the positive and only then say what might have been done better. Craig Revel Horwood could learn a thing or two from Pendleton et al.

Schofield's charisma encouraged a number of local general practitioners as well as hospital doctors to become tutors in communication skills. They were helped by actors, trained and coordinated by Tamsin Heatley, a successful TV actor and daughter of Oxford legend, Norman Heatley – the biochemist who worked with Florey on the early trials of penicillin. Many years later and after significant development by Oxford alumna, Catherine Hood, the teaching of communication skills was taken over by the Department of Primary Care.

When the Practice Skills Project came to an end, the University could not let the teaching of ethics (or communication skills) cease - thanks to the GMC's *Tomorrow's Doctors*. Weatherall pushed for a University Lecturer post to be created. Martin Vessey, the Professor of Public Health, provided space as well as wise and kind support. Thus, in 1995, for the first time, the University had a tenure-track senior position in medical ethics to which I was appointed. It was time to expand the activities to include not only teaching but also research, and ethics support to the NHS. The latter activity had already started.

Each government, it seems, has to put its imprint on the NHS rather as a dog marks its territory. In the early 1990s, due to yet another NHS reorganisation, general practices were given the responsibility for managing a large proportion of the NHS budget. The doctors at a local practice, realising they would face significant ethical issues in allocating resources, asked for help in developing a process and the guiding principles. I felt the need for proper philosophical input and approached Roger Crisp, whom I had met at a psychiatric seminar. He agreed to help. And so, it was that an Oxford philosopher, a specialist in Aristotle, came to roll up his sleeves and work at the coal face with primary care doctors to help in making practical decisions around resource allocation in real health care.

Further NHS reorganisation led Sian Griffiths, the Director of Public Health, to set up a resource allocation committee for the whole of Oxfordshire. Five years later, a national committee (known as NICE) was established to make decisions about resource allocation in health care covering the whole country. That committee borrowed many of the ethical principles and processes that had been developed in Oxford.

A small group discussion at Global Health Summer School in Vietnam. © Dinnah Rippon

Ethics support in clinical settings began when Anne-Marie Slowther came to Oxford. Slowther established a national network of clinical ethics committees to share experience, develop standards of good practice and provide training. There are over 100 committees in the UK and the network has become a model for developments in other countries such as Norway and New Zealand. Slowther is now Professor of Medical Ethics at Warwick Medical School.

Developing ethics research needed more resources. The only funded posts were that of the University Lecturer and the administrative assistant, both part-time. 'You need to call yourselves a Centre' was Muir Gray's advice. But how can one lecturer and an administrator be a centre? Muir Gray's answer was immediate: '*Headed notepaper. First, decide on a name. Second, get some good quality notepaper. Third, design a letter head with the centre's name and contact details at the top, and the names of some well-connected people from your advisory board at the bottom. Send out all your letters on that notepaper and see what happens.*' This was in the 1990s. These days the notepaper would be replaced by a website.

We chose a name: *The Ethox Centre*. Some thought it sounded like a chemical, but it included 'ethics' and 'Oxford' in a simple word. We designed the notepaper. Soon, with considerable help from John Ledingham, one of the great figures in Oxford medicine, and from Caroline Miles, the Ethox Centre received its first major donation: £500,000. Miles' experience in the public and private sectors proved crucial. Had the money been given directly to the University there would have been two undesirable consequences. First, a large proportion would have been creamed off. Second, the University would have set up a managing group of senior medical and surgical professors. That group would have controlled how The Ethox Centre could spend what remained of the donation. Many of those professors were antagonistic to medical ethics. Miles advised setting up an independent charity and appointing supportive trustees. She gave another piece of sound advice: '*Don't hoard the capital to live off the interest. Spend the money over three to five years employing people who will carry out interesting research. Only by doing good work will the Centre raise further money.*'

That first donation was used in part to create a research post. The successful applicant was Michael Parker. The research until Parker's appointment had been focussed on issues relevant to clinical medicine: Jacinta Tan and Anne Stewart's work on anorexia nervosa being one example. Parker started working with clinical geneticists and that led to his becoming involved with medical scientists. A few years later, Mikey Dunn was appointed. He developed the medical student teaching and also expanded the clinical research to include ethical issues arising in care homes. He is now professor at the University of Singapore.

Professor Michael Parker with colleagues in Kilifi, Kenya. © Dinnah Rippon

As Caroline Miles predicted, the more work we did the more funding we were given. The snowball got bigger. As the research increased, so more and more bright people from around the world applied to work with us, such as John McMillan, now Professor of Bioethics at Otago University.

The Centre grew, the work increased. I was talking with Bill Fulford one day and he said, '*think early about succession planning.*' I was many years from retirement, but I had seen research centres dwindle to nothing after the original director retired. If Ethox was to prosper in the longer term it would need a new director. And why wait until I retired? So, I stood down and Michael Parker became the second Director of The Ethox Centre. He has greatly expanded the activities in ethics and medical research. The Centre now has a particularly strong interest in collaborative global research and the ways in which such research can be ethically and effectively carried out in low and middle-income countries. Bursaries are provided to help build capacity in bioethics in these countries. Under Parker's leadership, many at Ethox work closely with Rory Collins and others in the Big Data Institute in the Department of Population Health, where Ethox is housed. In collaboration with the Berman Institute of Bioethics at Johns Hopkins, Ethox has established a major initiative in ethical issues relating to infectious diseases from a global perspective (GLIDE). Over the last two years, Parker has served on the Government's coronavirus advisory group, SAGE, and many in Ethox have been involved in projects related to the pandemic.

At its origin, Ethox staff could fit round a small table in The League of Friends. There are now over 50 staff including a dozen research students.

The Uehiro Centre's history has been very different from that of The Ethox Centre. The seed was planted on 06 August 1945 when Hiroshima was destroyed by the atomic bomb. A young man, Tetsuhiko Uehiro, not yet 40 years old, was exposed to high levels of atomic radiation. For months his life was in the balance. He survived. He responded not with rancour but with resolution. He founded a movement in Japan – the Practical Ethics Association. This Association, now with over one million members and almost 750 venues, unites people in a daily practice of morning meetings that focus on ethical and harmonious living. Tetsuhiko Uehiro died in 1972 and his son, Eiji Uehiro, took over as Chairman of the Association. In 2016, Eiji Uehiro's son, Tetsuji Uehiro, became the third Chair of the Association. In 1987, Eiji Uehiro established *The Uehiro Foundation on Ethics and Education* and appointed Noboru Maruyama as Director. The Foundation supports initiatives and projects in practical ethics at all levels of the Japanese education system.

One night, in 1999, my phone rang. The caller asked me if I would be interested in a multi-million-pound donation to the University of Oxford in support of practical ethics. He explained that he was 'our man in Tokyo' – David Morris, then head of the University's Japan Office. I didn't even know, at the time, that the University had a Japan office. Morris explained that there was a Japanese Foundation potentially interested in funding work in practical ethics at the University of Oxford. Would I meet with the Director of the Foundation? Still half asleep I said: 'Should I come to Tokyo now?' Morris said that the Director would come to Oxford.

That is how I came to meet Noboru Maruyama - at the Bath Place Hotel just outside the medieval city wall off Holywell Street. We walked round New College garden and talked about the novels of Agatha Christie. Christie's second husband, Max Mallowan, had studied at New College. Dr Maruyama proved to be extraordinarily knowledgeable about British crime fiction. Indeed, he was an afficianado of the *Morse* series which was on Japanese TV at the time, and which contributed to his love of Oxford. Years later, Colin Dexter, the author of the Morse novels, was made an honorary fellow of St Cross College. Dexter and Maruyama enjoyed several dinners together.

Maruyama met the Heads of several colleges and senior members of the Philosophy Faculty. The outcome was that in 2002, the Uehiro Foundation established *The Uehiro Chair in Practical Ethics*, associated with St Cross College. Julian Savulescu, a qualified doctor as well as philosopher, who had studied with Derek Parfit, was appointed to the Chair. In 2003, with further funding, *The Oxford Uehiro Centre for Practical Ethics* was created within the Philosophy Faculty. Under Savulescu's direction, the Centre has rapidly established itself as a world leader in research in philosophy and practical ethics. Roger Crisp is a Uehiro Fellow. Medical ethics is one significant strand of the work of the Centre under the direction of Dominic Wilkinson who works also as a consultant in newborn intensive care at the John Radcliffe Hospital. The Director of Research and Development is Thomas Douglas, also a qualified doctor.

Two Japanese students now come each year to St Cross College to study at the Uehiro Centre. One of these students told me that when his grandmother heard that he had won a scholarship to Oxford she turned pale. 'What is wrong?' he asked. 'Don't go to Oxford' she replied. 'Why not?' 'There are so many murders in Oxford, and if it wasn't for that nice

Inspector Morse there would be many more.' The student had had to promise his grandmother that he would never be out on the streets after 9pm.

The greatest pleasure for anyone who has taught Oxford's medical students is to meet those students again, years after they have qualified. There is such variety and richness in the lives and careers of our medical alumni that I find it inspiring, even in retirement. I recently met with Mehrunisha Suleman whom I remember as a lively contributor to the seminars in ethics when she was a student. She had just been appointed as the Research and Public Engagement Lead at Ethox. When I was an undergraduate, Henry Harris, later Regius Professor of Medicine, told me that the hallmark of Oxford was that most of our teachers were also world-class researchers. Thirty years ago, when the first course in ethics for clinical students was delivered, there was little medical ethics research. The course will now be led by Suleman, a world-class researcher, with support from others in the Ethox Centre. Ethics in Oxford medicine is now mature: teaching and research are firmly integrated, together, hand-in-hand.

The Ethox Centre: www.ethox.ox.ac.uk
The Uehiro Centre: www.practicalethics.ox.ac.uk
The Wellcome Centre for Ethics and Humanities: www.weh.ox.ac.uk
GLIDE: www.oxjhubioethics.org

Staff of the Uehiro Centre. © Rocci Wilkinson

The Dark Art of Monitoring Clinical Trials

Professor Tim Peto
(1968 Brasenose College), Professor of Medicine and Co-Leader for the Infection Theme of the Oxford Biomedical Research Centre

My Introductions into Clinical Trials

My first exposure to clinical trials was in the early days of AIDS. I was a clinical lecturer to David Weatherall. In 1987, David Warrell was asked to chair an MRC Committee to advise on undertaking clinical trials on AIDS and he in turn asked me to be the 'scientific secretary' to the Committee. This was a role that he made up without a clear job description. I took it to mean that I could say whatever I felt like at the Committee and do nothing. Two hundred and eighty-two patients were randomised: half were given AZT and half placebo. Although only 27 patients completed the 24-week planned follow, the Data and Safety Monitoring Committee (DSMC) stopped the trial early because 19 patients had died in the placebo arm and only one in the active arm. Amidst major publicity, the world considered that AIDS was now treatable. I rang up my namesake, Richard Peto (the world's leading clinical trialist, also in the NDM), to discuss the early stopping and he endorsed the results saying that the results were so extreme they could not have occurred by chance.

As we now all know, AZT monotherapy stopped working because of the development of resistance. We in the MRC, together with French colleagues, undertook a trial (Concorde) to determine whether starting AZT in early disease would work better. In parallel, our US cousins undertook a similar trial. After a year, the US again stopped the trial early because of efficacy whilst our DSMC continued our trial. This difference of opinion between DSMCs triggered huge controversy, especially when two years later the final results from Concorde showed no benefit from early treatment. Five years later, triple therapy became available, providing long term benefit.

My First DSMC Experience

In 1990, Nick White (now Professor Sir Nick White) asked me to be the 'WHO monitor' of a blinded trial he was conducting in Vietnam comparing a new drug artemether with quinine (AQ study) for the treatment of severe malaria. I was delighted. I was given no instructions but was given the randomization code and asked to do the analysis myself and to advise the trialists whether to stop the study. I visited Ho Chi Minh City and checked the randomization procedure. I entered a darkened room to find an Oxford medical student crouched on the floor putting active drug into one set of boxes and placebo into another set. He assured me he was keeping careful records and not getting the boxes mixed up. He convinced me that he was the man for the job. His name was Chris Whitty. When this small study ended, there was only marginal evidence that artemether was better than quinine.

How do DSMCs Work

Since then, DSMCs have become better organised. The funders approve the members and the Committee follows a charter. They are independent and therefore are not generally authors of the publication. However, there is still no formal training for this role. The investigators remain blind to the study arms and the DSMC approves the analysis plan before any data is available. This is to ensure that investigators, some of whom are heavily invested in one study arm being superior to another, can be protected from accusations of possibly interfering, intentionally or unintentionally, with the study to get a result they want.

The DSMC's role is to see the actual data in real time. The first part of the meeting is 'open' and the trialists update the DSMC of the progress of the trial and share any concerns about any external hindrances to the study. The closed meeting data is presented by the trial statistician. The DSMC has a number of roles. They clearly need to protect study patients, both after enrolment and who plan to enrol, from possible harm. They also need to consider the possible societal benefit of the new treatment to patients not in the study who would benefit if the treatment were adopted nationally. In addition, funders and trialists need protection from the cost of wasting resources if a trial is stopped too early preventing the trial giving a clear result. The DSMC also has a role of an experienced 'critical friend' advising on data integrity, data collection, methods for the unbiased ascertainment of end-points and analysis plans.

Trial protocols plan to recruit a pre-determined number of patients for a pre-determined period of time. In most cases, the trial reaches its natural end and during the trial, the DSMC simply reports that 'they have no safety concerns and recommends that the trial should continue 'as planned'. However, sometimes a difference between the two study arms gradually emerges. The DSMC has then the challenging task to monitor the differences and decide when, if ever, to stop the trial early. DSMCs only stops a trial early if they consider that there is evidence 'beyond reasonable doubt that one arm is superior to another such that it will change clinical practice'.

At the meeting, DSMC members have two main anxieties and opportunities for making major mistakes. They might allow a study to continue too long when it is quite clear that one arm is superior to another and could be criticised for causing harm, or even death, to trial participants. Alternatively, they might be over-cautious and stop a study when, on reflection, there is no convincing difference between the study arms. The DSMC could then be criticised for wasting time and money and missing an opportunity to identify a new effective treatment.

When I started, I played on an excel spreadsheet using a random number generator and learnt that, even with no differences between study arms, one arm often has a lucky run showing an apparent difference. I learnt that studies should continue until there is virtually no chance of stopping a trial merely because of a lucky run.

Examples of DSMC Decisions

Over the last 20 years, I have chaired about 30 DSMCs of major trials. We have given overall reassurance and support to the trialists and sometimes made suggestions to improve the design or conduct of the study. However, on a few notable exceptions, the DSMC recommended that the trial should deviate from the planned protocol.

Unexpected Outcomes

In 1999, children with severe malaria were randomized to routine prophylactic phenobarbital or placebo to determine if it would reduce the overall frequency of fits and subsequent brain damage. The interim analysis, just before the planned end of the trial, showed that apart from the expected reduction of fits, there was an unexpected possible increase in mortality which was not statistically significant. The DSMC decided to extend the trial for a further season to determine whether the increased mortality was only a statistical wobble. A year later, the mortality difference was confirmed and the treatment was rightly abandoned even though it had succeeded in reducing seizures. The extension of the trial avoided the possibility that the mortality increase would have been disregarded as 'unexpected and insignificant' allowing the use of a dangerous treatment.

Duration of Action

In 2003, the MRC studied the efficacy of co-trimoxazole (septrin) on survival of HIV infected children without access to HIV treatment. After six months of treatment, co-trimoxazole clearly halved mortality. However, the DSMC decided not to stop the study at that stage because it was felt results from a short-term study were insufficient to change guidelines for long term use. At the next interim analysis, after a median follow up of 19 months, the reduction in mortality persisted. The DSMC stopped the study. The results were considered convincing and National Guidelines were changed protecting children until HIV whilst awaiting HIV treatment. Interestingly, no-one complained that the trial went on too long.

Generalisability of Result

In 2005, the Oxford Wellcome Trust Unit in Bangkok organized a study comparing aquamat with quinine against severe malaria in four countries in Southeast Asia. After one year, the results found clear evidence that aquamat was superior. However, most of the difference were found in the results from Myanmar. The DSMC felt that rational sceptics might be concerned about the generalisability of results from one centre with little experience of clinical trials. The trial was therefore continued for another season: aquamat was clearly superior in all countries and the DSMC then stopped the trial. The trial resulted in artesunate being widely adopted for adult treatment of malaria and also provided the justification for the funding of a similar study in African children which showed the same effect leading it to be adopted worldwide.

Conclusions

I have given some examples of DSMCs changing the course of a trial. In other cases, we quietly allowed trials to continue to optimize the chance of a convincing result. Many novice DSMC members are understandably anxious whenever there is some evidence of harm. My role has been to aim to remain calm and find a counter-argument to persuade the committee that the trial should continue. I have found this work immensely rewarding, sometimes very exciting.

What Have We Learned About Immunity to SARS-CoV-2?

Professor Susanna Dunachie
(1991 New College), NIHR Global Research Professor, Honorary Consultant in Infectious Diseases and Medical Microbiology, University of Oxford

Covid-19's colossal impact on excess mortality, our personal and professional lives, and the well-being of our fellow citizens, raises questions about lessons for the future. Observing the spread of a novel pathogen in an unexposed global population has been a painful experience. The long-term sequelae of SARS-CoV-2 are unknown. Many people (including children) are suffering "Long Covid" so research is essential.

Although the UK stands out for its continuously high rates of infection, the UK's contributions to knowledge from high rates of testing, world-leading genomic surveillance, the open sharing of accurate data, high vaccination rates, and driven, collaborative scientists in academia and the public sector are reasons to be proud. The UK's giant national "SARS-CoV-2 challenge study" has given the world numerous insights into immunity to SARS-CoV-2. Oxford University scientists have collaborated in an unprecedented effort to counter the virus (Box 1).

SARS-CoV-2 is the seventh coronavirus to infect and cause disease in humans. At the start of the pandemic, immunologists considered existing knowledge from other coronavirus infections. Severe acute respiratory virus (SARS) and Middle East Respiratory Syndrome (MERS) were already recognised threats. SARS was rare and disappeared by 2004, perhaps through a combination of luck, excellent containment policies in Asia, and the transmission dynamics of SARS including the fact that only symptomatic subjects were infectious. MERS still exists but has not spread significantly outside the Middle East. There are also four "seasonal" or "common cold" human coronaviruses (HCoV) which cause mild coryzal illnesses world-wide with most people developing antibodies to all four during childhood.

Studies were set up in Oxford and elsewhere to measure the immune response to SARS-CoV-2. The spike protein is a relatively conserved and immunogenic molecule studded across the surface of the virus, and the target of all the vaccines currently licenced in the UK. Antibodies to spike can play several roles including neutralisation, complement activation, and binding to cell surface receptors to enhance viral clearance. T cells direct the immune response (including B cells to make antibodies) and kill infected cells. In addition, mucosal immunity in the nose and respiratory tract is likely to play a key role in early defence through innate immune responses and local IgA antibody production.
Here are seven initial hopes for the immunology of SARS-CoV-2, and what we have learned so far:

Box 1: Oxford University's Contribution to Knowledge on Immunity to SARS-CoV-2

- The Oxford/AstraZeneca vaccine
- COVID-19 Viral Challenge Study
- RECOVERY & other hospital-based drug therapy trials
- PRINCIPLE, PANORAMIC, ATOMIC & other community-based therapy trials
- Test development: antibodies (including haemagglutination assay), PCR tests & evaluation of lateral flow devices (LFDs)
- C-MORE & "Long COVID" clinical, immunological & imaging studies
- Humoral immunity including neutralisation
- Inflammatory Response
- T cell research
- Deep Phenotyping including COMBAT
- Data Integration & Analysis – ISARIC, OpenSafely, Office of National Statistics analysis on antibodies and vaccine effectiveness
- Vaccine response including PITCH & OCTAVE

And many many more
https://www.ouh.nhs.uk/research/projects/covid-19/

1. Silent Acquisition of Immunity
We hoped to see rapid asymptomatic seroconversion, that is high rates of antibodies in the general population who were not aware they had been infected. This had been the case (to a certain extent) with swine flu but sadly, this was not observed for SARS-CoV-2 in the UK. Only six per cent of adults in England had antibodies by July 2020 (an effect of lockdown), indicating we had a very long wait for population immunity.

2. Immunity after Covid-19
Another hope was that healthy people who had suffered Covid-19 would never catch it again, rather like the measles. We had clues this might not happen from existing studies of the common cold coronaviruses, which demonstrated that people's antibodies wane and re-infections are frequent after about a year. Now we know that re-infection with SARS-CoV-2 is not a rare event, although the effects tend to be mild. Our healthcare worker study and others have found not only a large and unpredictable variation in the strength of the immune response after SARS-CoV-2, but that immunity wanes. However, people who had infection followed by vaccination develop highly desirable "hybrid immunity" greater than after infection or vaccination alone. Whether exposure to virus after vaccination can boost and extend immunity is under study.

3. Vaccine-acquired Immunity
It was hoped that vaccinated people would not catch or pass on SARS-CoV-2. In fact, "vaccine breakthrough" infections are now commonplace. People who have had two doses of UK-licensed vaccines are much less likely to catch SARS-Cov-2 but can still acquire the infection and transmit it.
The UK is now rolling out "booster" third doses of vaccines which will hopefully greatly reduce the number of vaccine breakthrough infections this winter. VIBRANT is an Oxford-led collaboration with UKHSA and other universities of the immune responses associated with vaccine breakthrough to help identify people at risk.

4. Optimal Vaccine Strategies
At the end of 2020, the UK government took the brave but science-based decision to deliver two doses of Pfizer/BioNTech or Oxford/AstraZeneca vaccine 12 weeks apart. This doubled the number of people who could rapidly benefit from the relative protection against severe disease that one dose gave, but left people temporarily exposed without the higher protection of two doses. The UK "got away with it" for high-risk people before the surge of infections from the Delta variant. Our PITCH* study showed that the longer dosing interval actually produced higher antibody levels and a T cell response associated with improved memory. Further studies from UK and Canada confirmed greater vaccine effectiveness from the longer dosing interval.

5. A Vaccine for All
The vaccines licenced in the UK are all remarkably immunogenic, including in older people. However, ongoing studies including OCTAVE, suggest that some groups of patients have a poor antibody response to vaccines. These include transplants recipients who are immunosuppressed, and people receiving immunomodulatory therapies which block B cell antibody production. Identifying people with low responses will allow different vaccination and management plans for them (such as administration of monoclonal antibodies and emerging antivirals such as Merck's molnupiravir and Pfizer's paxlovid). Mucosal vaccines in clinical trials (akin to the intranasal flu vaccine) may show further benefits. Only six per cent of Africa's sub-Saharan population is fully vaccinated and, from both a humanitarian and global health security perspective, this inequity must be remedied.

6. Herd Immunity
The "herd immunity threshold" (HIT - the level of immunity required in the population to prevent the infection from spreading) remains elusive. Herd immunity is extremely important to protect vulnerable people in the community whose immune systems may not respond to the vaccine. In autumn 2021, the Office of National Statistics estimated that 93 per cent of the adult UK population have antibodies to the spike protein of SARS-CoV-2, and yet we still have a high UK prevalence of SARS-CoV-2. It is still not known whether anti-spike antibody levels are a good marker of immunity to SARS-CoV-2. Cellular immunity, while more difficult to quantitate, may be just as important. HITs for other infections such as measles can be very high and may require 95 per cent of the population (including children) to have antibodies to prevent outbreaks. To reach SARS-CoV-2's HIT, acquisition of immunity from past infection and vaccines needs to outpace waning immunity. Variants with higher transmission rates, such as delta raise the HIT. There was speculation that the UK's undergraduate student population may have reached the HIT for delta given how few of the current cases this autumn on campuses are in undergraduates compared to the large outbreaks the first term of the previous academic year.

7. Variants of Concern
In early 2020, some experts predicted that the SARS-CoV-2 virus would not mutate very much. This was one of the surprises of the pandemic. "Variants of concern" such as the Delta variant, emerged by the end of the year. Current vaccines remain highly effective against all variants to date and continue to give good protection against severe disease, although prevention of any infection is reduced. The latest concern is the Omicron variant. We are learning about how much it impacts on transmission and how much viral escape Omicron has for vaccine or infection-acquired immunity. The new antiviral therapies should be unaffected.

> *"there is still much to learn about immunity to SARS-CoV-2 including the spectre of Omicron. We should focus on minimising harms such as Long COVID, and risks to the immunocompromised.*

Conclusions
There is still much to learn about immunity to SARS-CoV-2.

- We should focus on minimising harms such as Long Covid, and the risks to the immunocompromised.
- Protection against Covid-19 may depend on a mixture of non-specific defence mechanisms, adaptive immunity (antibodies and T cells to SARS-Cobv-2), the environment (ventilation, and humidity levels) and the "bioburden" (number of infectious virus particles encountered) as well as chance.
- Humans probably haven't evolved to have sterile immunity (100 per cent protection against any infection to respiratory viruses). Many respiratory viruses infect young children and the majority experience mild illness in their early years before acquiring sequential immunity to render subsequent infections mild while the virus circulates indefinitely.
- SARS-CoV-2 may be destined to be the fifth "common cold" coronavirus, but such immunity is hard-won in a globally naïve population and may take decades to equilibrate, even with effective vaccines.
- Whether these will give lasting protection after a three-dose strategy, or whether everyone will need a booster for omicron once available and future annual boosters remains to be seen.

Meanwhile, we must own up to our wrong calls hope the waves in the stormy seas of the pandemic diminish so we can once again stand confidently on deck.

A health worker volunteers for our Covid-19 Immunology Study.
Photo by Prof Ellie Barnes.
*PITCH *(Protective Immunity from T cells to Covid-19 in health workers) consortium*
www.pitch-study.org

Recent Advances in Asthma Treatment

Dr Timothy SC Hinks
(1998 Wadham College), Wellcome Trust Career Development Fellow and Honorary Consultant, Nuffield Department of Medicine, University of Oxford

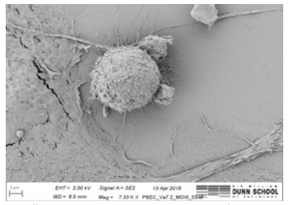
The last decade witnessed a revolution in how we understand and treat asthma. The world's most common lung condition was perhaps described in Chinese medical literature c 2600BC[1], and Homer used the term 'asthma' – ἄσθμα – in his *Iliad*[2], a term adopted in English since around 1600[3]. Treatments were limited but in the ninteenth century, the Dorset born physician, Henry Hyde Salter, eloquently described the condition from which he suffered and his self-medication with coffee, no doubt benefitting from bronchodilation from methylxanthines[4,5]. He could also have smoked Datura *stramonium*[6], an anticholinergic: both forerunners of treatments twentieth century bronchodilators. Last century saw only two major new classes of treatments: ephedrine in 1928, leading to a whole family of increasingly selective and long-lasting beta-adrenoreceptor agonists, and steroids given systemically in 1949 and by inhalation from 1972. For those with severe asthma life was miserable, and often limited. Older patients remember being in special schools for asthmatics and witnessing friends dying from attacks. Steroids and beta-agonists certainly made a vast difference to most patients, though as a registrar I had little to offer those with severe disease, beyond ever escalating doses of inhaled corticosteroids. The clinic had a reputation for patients with either poor adherence or insoluble clinical problems. Just 10 years later, the outlook now is very different, for four reasons.

First, clinical phenotyping and biologics. Not all asthma is the same. My colleague, Ian Pavord, described the severe eosinophilic phenotype: people with adult onset, severe disease, which responds dramatically to systemic steroids, characterised by excess eosinophils in sputum and blood. This observation rescued a whole class of drugs-the anit-interleukin (IL)-5 monoclonal 'biologics' from failure in trials. Targeted to the right patient, based simply on a full blood count eosinophilia, these produce dramatic improvements, reducing exacerbations by three-quarters, and obviate the need for maintenance steroids. We treat over 300 patients on these monthly or bimonthly subcutaneous injections: patients who typically describe them as 'transformative'. Five biologics are now licensed targeting the three pathways: immunoglobulin E, the IL-5 pathway and the IL-4/13 pathways. Benralizumab acts so fast our team – in a trial led by Mona Bafadhel – are testing its use first line for acute exacerbations, in asthma and chronic obstructive pulmonary disease. If successful, these drugs will consign systemic steroids to the history books.

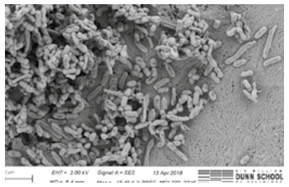
Secondly, the multi-disciplinary team. For too long for those with 'difficult asthma', the elephant in the room was poor adherence. Now our Sherlock Holmes pharmacist has scrutinised prescription records before I first meet the patient. Adherence is addressed non-confrontationally with the aid of a home FeNO suppression test. Fractional exhaled nitric oxide directly measures interleukin-13-mediated airway inflammation in exhaled breath, which takes 10 seconds to measure by a simple hand-held device. Patients with high FeNO take home a micro-chipped inhaler and FeNO monitor for a week. In two thirds with poor adherence, FeNO falls, symptoms improve, and we offer smart phone synchronised inhalers: problem solved. The other third, whose FeNO remains stubbornly elevated, have steroid-unresponsive disease and need biologics, short-cutting months of ineffective medication changes. Another key MDT member is our speech and language therapist, identifying and treating laryngeal wheeze. Such vocal cord dysfunction is terrifying, leading to inappropriate treatment, recurrent admissions, and on occasion intubation. Likewise, many symptoms are due to breathing pattern disorders, which are debilitating – think Emma Raducanu exiting Wimbledon – but are effectively treated by our physiotherapists.

Thirdly, macrolides. I'm always looking for another 'treatable trait': persistent bacterial bronchitis. Those with a chronic mucopurulent cough and 'type-2 low' asthma invariably have lower airway colonisation with non-typeable Haemophilus influenzae, with a striking response to long-term, low dose macrolides. The mechanisms underlying this drug's unique antibacterial, antiviral and anti-inflammatory effects are a major current focus for my research group, using infection of air-liquid interphase cultures, bacterial metagenomics and single cell sequencing of bronchoscopy samples.

'A patient's experience of living with asthma. Marije Kootstra, 2011 reproduced with permission from herself and U-BIOPRED'



T cell PBEC Va7.2 MO10 'A mucosal associated invariant T cell interacting with primary human airway epithelial cells. 7,333 x magnification scanning electron micrograph by Maisha Jabeen.'



'Haemophilus influenzae colonising primary human airway epithelial cells. 15,000x magnification scanning electron micrograph by Maisha Jabeen.'

Fourth, ditching salbutamol. Asthma still kills three people per day in the UK. The National Review of Asthma Deaths found over-reliance on short acting bronchodilators a major contributor[7]. When asthma treatment is separate inhalers of salbutamol providing rapid symptomatic relief, and slower-acting inhaled steroids which reduce mortality, inevitably many people reach for the blue inhaler and give up with the brown. Four large RCTs found replacing separate inhalers with combination formoterol/budesonide inhalers reduces symptoms and hospital admissions, even in mild asthma[8]. Our Oxfordshire guidelines now favour this approach, and we expect national guidelines to follow.

Greening the NHS

In light of COP26, it's heartening to know our guidelines will play a major part in greening the NHS. Chlorofluorocarbon propellants in previous pressured metered dose inhalers (pMDIs) were withdrawn due to destruction of the ozone layer. Unfortunately, current propellants are powerful greenhouse gasses. The propellant HFA227ea is 3,320 times more potent than CO2. One Ventolin inhaler has a carbon footprint of 28kgCO2e per inhaler: equivalent to a round trip from Oxford to Leicester in an average car. Incredibly, pMDIs in UK are responsible for 3.5 per cent[9] of the entire NHS carbon footprint. A switch to a dry powder preparation, favoured in our new guidelines, will reduce that by 94 per cent[10].

The Future

The biologic revolution continues. The next generation will target alarmins like IL-25, IL-33 and TSLP, molecules produced by damaged airway epithelium which initiate the type-2 inflammatory cascade. Acting further 'upstream' they are likely to be potent and treat a wider range of biological phenotypes. Further advances will require new understanding of the complex immunological puzzle that is asthma. My group analyse the transcriptome and epigenome of airways tissue obtained at bronchoscopy on a single cell level, use whole genome sequencing to define rare phenotypes of asthma, and spatial transcriptomics to map where inflammatory proteins and lipids originate. We are now growing airway epithelial cells from induced pluripotent stem cells. On the further horizon might be cures for asthma. Asthma develops from the complex interplay of gene and environment and so must depend on epigenetic changes. We are analysing the airway epigenome at single cell resolution to identify those switches. Already there are nine epigenetic therapies with FDA approval for other conditions, so I'm optimistic the pace of change will only accelerate during my research career.

Seeking Research Volunteers

For now, my team are always looking for healthy research volunteers to match our older asthma patients – do drop me an email if you'd like to hear more. And outside the lab, there remains an urgent need to improve air quality for the world's urban populations and to make these life-saving, but basic dry powder inhalers affordable globally, where today asthma affects >350 million people and inflicts 400,000 deaths a year[11], deaths we have the technology to prevent, given just a little bit more commitment from wealthier nations.

www.ndm.ox.ac.uk/team/timothy-hinks
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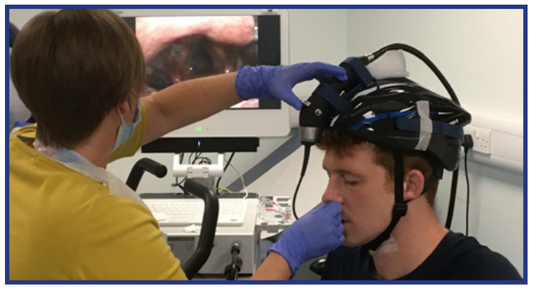
@HinksLab

The Hinks Lab Group

The Oxford asthma MDT 'The Oxford Special Airways Multidisciplinary Team'



'Performing continuous exercise laryngoscopy to diagnose exercise induced vocal cord dysfunction'

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A Breath of Fresh Air: Integrated Respiratory Medical Care

Dr Will McConnell
(1988 Green Templeton College), Respiratory Consultant, Dorset County Hospital NHS Foundation Trust

On becoming a respiratory consultant in Dorset 20 years ago, the first instruction from management in the hospital was to discharge more patients from follow-up. But I had no idea about the skills, capacity and systems for managing these patients in primary care. If a patient deteriorated, who would notice and where would they get help. It was clear that there were some areas of excellence within the community, but other areas seemed to struggle to provide optimal respiratory care. Since then, one of my ambitions has been to identify and target those areas of greatest need and improve care in the community, enabling me to discharge patients safely or even prevent their referral. No matter how wonderful we make our secondary care services, we are still only scraping the surface of respiratory care across the population. Teaching sessions have limited benefits, only by reaching a small proportion of community staff with rather short-term benefits. How could I get deeper under the skin of primary care and work in a more integrated way to really improve outcomes?

With my colleagues from neighbouring hospitals, we created an outreach team of nurses to support patients with COPD and asthma in the community, aiming to reduce admissions and facilitate discharge and to deliver pulmonary rehabilitation and oxygen assessment services for the community. This service, commissioned by what was then the Primary Care Trust, still felt as if it floated over primary care, rather than being embedded within it. When Lansley's Health and Social Care Act in 2012 created Clinical Commissioning Groups, secondary care providers were excluded from influencing the commissioning of services and a more market-driven, competitive environment for healthcare was fostered with an emphasis on payment by activity, rather than improving outcomes by working together to develop better systems. Efforts for greater collaborative working seemed hopeless.

But I was lucky to be working in Dorset, because the effects of the Lansley reforms did not endure for long there. Dorset CCG soon realised that a collaborative approach would be essential to improve outcomes and contain costs. Input from the providers of care was crucial to redesigning the pathways of care. The NHS providers of Dorset took the bold step to move away from contracts based on payment-by-activity to block contracts, thus completely changing the incentives for organisations within the system.

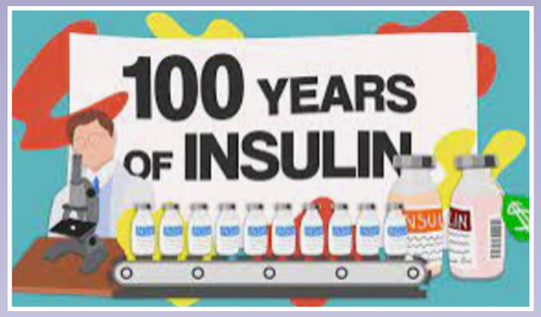
The Government volte-face, encapsulated in the Five Year Forward view and then the NHS Long Term Plan of 2019, has made working together de rigueur and clinicians have a voice. Covid-19 has exemplified the benefits of this working – delivering the changes required for the NHS to cope with the pandemic would have been impossible if we had to wait for formal commissioning processes and market forces to determine the outcome. So now I find myself as Clinical Lead for a new Dorset Respiratory Clinical Network and a Clinical co-lead of the even newer South West Respiratory Network. We are now practising Population Health Management for our respiratory patients. I have access to data about every asthma and COPD patient in Dorset. I can see where the areas with poor respiratory outcomes are, and which surgeries seem to be struggling. I can drill down to pseudonymised individual patient-level data and identify proactively those patients who could benefit from more detailed assessment in secondary care or from more advanced treatments, such as biologics for asthma. We have respiratory nurses embedded within most of our Primary Care Networks to lead the changes and support the primary care teams. I hold monthly MDT meetings with the PCN teams to discuss patients who are struggling with their disease and I see patients in GP surgeries with little waiting time, outside the traditional referral processes. We are creating Respiratory diagnostic hubs within the PCNs where patients can access the right diagnostic tests in a timely fashion delivered by skilled practitioners. I can access their primary care records in the hospital, so I can tell what treatments have been tried, how frequently they are exacerbating, whether they are claiming their preventer inhaler prescriptions. I know that the skills, capacity and systems exist in primary care to care for most respiratory patients. And if a patient deteriorates, we have systems that will notice it, and staff in the community with the skills to deal with it and with access to support from secondary care.

So, finally, I think I can discharge a patient from follow-up.

Weymouth from Portland

100 Years of Insulin - A Lifesaving Drug and Murder Weapon

Dr Neil Snowise
(1974 Corpus Christi College), Visiting Senior Lecturer, Institute of Pharmaceutical Science, Faculty of Life Sciences and Medicine, King's College London



Murder by healthcare workers using insulin continues to this day. This year marks the centenary of the discovery of insulin, which was one of the twentieth century's greatest medical discoveries. Before 1921, it was exceptional for people with type 1 diabetes to live for more than a year or two.

Frederick Banting was given laboratory facilities by J.J.R. Macleod, the Head of Physiology at the University of Toronto, to investigate the function of the Islets of Langerhans. He brought in a research student, Charles Best, to assist him with his experiments, isolating insulin in 1921 and demonstrating its benefits to reduce the hyperglycaemia in dogs made diabetic by removal of their pancreases.

Earlier work with pancreatic extracts had resulted in toxic reactions due to impurities. Macleod invited a biochemist, James Collip to assist and he subsequently purified insulin, so it would be safe enough to be tested in humans, leading to great therapeutic success.

In recognition of their life-saving discovery, Banting and Macleod were jointly awarded the 1923 Nobel Prize in Physiology or Medicine, although this was contentious and increased the animosity between them; subsequent opinion was that Best should have shared the prize.

Best (left) and Banting (right) with one of the diabetic dogs used in experiments with insulin. © University of Toronto Archives

Murder Most Foul

The discovery of insulin revolutionised both the therapy and the prognosis of diabetes. Who would have envisaged that such a useful drug has also been used as a murder weapon, over many years and continues to be misused in this way? Serial murder by healthcare professionals is poorly understood but increasingly identified; a variety of methods have been used, of which insulin accounts for around 13 per cent, causing death through prolonged hypoglycaemia, when sufficiently severe. In a 2009 review, 66 cases of suspected or proven murder using insulin were identified from 10 countries and more have arisen since that date. A few of the healthcare perpetrators are doctors, but the vast majority are nurses.

This article looks at some examples of the more notorious cases where healthcare professionals have been convicted or accused of using insulin to murder others.

The first published case where the perpetrator was a healthcare worker was Kenneth Barlow, a registered nurse, in Yorkshire, in 1957. He murdered his pregnant 32-year-old wife, at home in the bath, trying to make out that she had unfortunately drowned by accident. His account of events was suspicious and a second examination of her body revealed two injection sites in each buttock. This was over 60 years ago when limited assays available to measure insulin relied on finding the dose of insulin which caused hypoglycaemic convulsions in mice. Extracts of tissues from the victim's buttocks were injected into mice, producing measurable quantities of insulin. He was sentenced to life imprisonment and released 26 years later, in 1984, still maintaining his innocence.

Advances in Toxicology

Toxicology can play a key role to provide evidence in many cases of suspected murder by insulin and has advanced significantly. Hypoglycaemia is the first clue to homicidal insulin use in living subjects, but valueless in victims found dead.

Pro-insulin is cleaved into two peptides, insulin and a smaller C-peptide. Insulin was not amenable to accurate measurement in biological fluids prior to the invention of immunoassay in 1960. C-peptide was discovered after immunoassay was invented and can also be measured now; a high level of C-peptide generally indicates a high level of endogenous insulin production. A low insulin: C-peptide ratio can provide invaluable evidence of exogenous insulin administration.

> *"Insulin has revolutionised diabetes treatment, but who could have envisaged such a useful drug also being used as a murder weapon?*

20th Century Serial Child Murders
Fast forward several decades to the infamous case of Beverley Allitt, a State Enrolled Nurse at Grantham Hospital. In 1991, several unexpected infant deaths and unexplained illness occurred on the children's ward where she worked. Initially, suspicions were raised at the tertiary referral hospital QMC, Nottingham, when referrals in a two-month period were over double the usual annual rate from Grantham. Painstaking investigations provided excellent evidence of insulin as the murder weapon, in at least two of the cases. With the more sophisticated analyses now available, assays revealed very high levels of immuno reactive insulin, accompanied by very low C peptide. These findings, along with Allitt's attendance during these attacks, finally led to her arrest. She was convicted of murdering four children, attempting to murder three other children, and causing grievous bodily harm to a further six. Sentenced to life imprisonment in 1993, she is currently detained at Rampton Secure Hospital. Perhaps the most notorious British serial child killer, Allitt was the subject of a book and a BBC dramatisation of the case, *Angel of Death* (2005).

Expertise from an Oxford Doctor and Scientist
One of the expert witnesses in the Allitt case was Professor Vincent Marks, who has a worldwide reputation in the field of suspected murder by hypoglycaemia. He had previously been an expert witness in the infamous case of British socialite, Claus von Bulow, at whose trial he testified in 1982 (and which led to his acquittal on a charge of attempted murder); since then he became increasingly interested in the forensic aspects of hypoglycaemia. Professor Marks has published widely, including a book '*Insulin Murders.*' He was an undergraduate at Brasenose between 1948 and 1952, after which he undertook his clinical studies at St Thomas's. A chemical pathologist, he became foundation Professor of Clinical Biochemistry in the newly established University of Surrey. He was also Head of Clinical Biochemistry and Consultant to the Clinical Investigation and Metabolic Unit at nearby Royal Surrey County Hospital.

He developed a simple method for measuring glucose at low concentrations in blood accurately, something that had previously not been possible in clinical practice. Furthermore, due to his interest and established record in immunoassay development and provision, he set up the first NHS laboratory

Professor Vincent Marks (1948 Brasenose College) - expert witness at many court cases of hypoglycaemic murder

in the UK to offer insulin assays as a national service. His last appointment was Dean of Medicine in the newly established Post-Graduate Medical School at the University of Surrey.

21st Century Cases of Murder by Insulin
The "Stockport Murders" reflected a different kind of healthcare worker serial killer, whereby the victims were seemingly chosen at random. Victorino Chua, a hospital nurse, injected insulin into saline bags and ampoules while working on two acute wards at Stepping Hill Hospital, Stockport, in 2011. He left these contaminated products in the treatment rooms, not knowing who would fall victim to his actions. These were then unwittingly used by other nurses on the ward, leading to a series of insulin overdoses. In 2015, he was convicted by a jury at Manchester Crown Court of murdering two patients and 22 counts of attempted grievous bodily harm alongside other charges.

During the three-month trial, no motive ever really emerged for why Chua decided to kill his patients. According to Professor Marks, who was consulted on this case, there was overwhelming evidence of foul play by the administration of insulin. However, his conviction was largely based on a long-handwritten note from the self-styled "angel turned evil," which was interpreted as a confession.

He was jailed for life and subsequently failed in his 2016 applications for permission to appeal against both conviction and sentence length.

There have been a cluster of convictions in New South Wales in recent years, for murder by insulin where the perpetrator was a health care worker. In completely separate incidents, all of which came to trial in 2016, two nurses were convicted, as well as a Sydney GP Dr Brian Crickitt. The 2016 trial was told that 63-year-old Crickitt killed his wife with a lethal injection of insulin so he could claim her life insurance and start a new life with his mistress. There were no traces of insulin found in Mrs Crickitt's body, but there was other evidence that led to his conviction. Crickitt had viewed webpages outlining the dose required for a lethal injection of insulin the day before her murder and had tried to hide his internet search history. The next day, he wrote a prescription for fast-acting insulin under another patient's name.

Professor Marks provided an expert report for the New South Wales State Coroner and felt that the evidence was all circumstantial. The possibility that she might have been injected with insulin leading to hypoglycaemia and death was raised because of the identification, many months after the event, from a photograph of the corpse taken post-mortem, of a possible injection site on her buttock. This illustrates the difficulties in proving a case "beyond reasonable doubt" when there is no laboratory or clinical evidence to support a diagnosis of death from hypoglycaemia due to insulin.

However, Crickitt was found guilty and sentenced to a maximum of 27 years in jail. He appealed in 2018, asserting that he suffered a miscarriage of justice as the Crown did not prove "beyond reasonable doubt" that insulin killed her. The court rejected all appeal grounds including that the guilty verdict was unreasonable or not supported by the evidence.

Crickitt is not the only doctor to be convicted of murdering his wife. Dr Colin Bouwer, a psychiatrist practising in New Zealand, was convicted of murdering his third wife in 2001. Allegedly, he drugged his wife to simulate the symptoms of a tumour. He used a combination of sedatives and hypoglycaemia inducing drugs, including insulin, obtained with forged prescriptions. More recently in 2018, in India, Dr Govind Prakash, a diabetologist, was reported to have killed his mother and sister by injecting them with an overdose of insulin and tried, unsuccessfully, to end his life by the same method.

Modern Toxicology is not 100% Fail Safe
Although scientific methods have advanced and assays for insulin and C-peptide can be invaluable to provide strong evidence for the prosecution, they cannot prove foul play with 100 per cent certainty. Raised insulin levels could indicate a rare medical condition (such as insulinoma) rather than a crime or the evidence can be unclear. One such relatively recent case is nurse Colin Norris, who was convicted of murdering four elderly patients and attempting to murder a fifth by poisoning them with insulin at two Leeds hospitals. He was sentenced to 30 years in prison in 2008. The jury at Norris's original trial was led to believe, by experts, that a cluster of hypoglycaemic episodes, among elderly people who were not diabetic, was sinister. In Professor Mark's expert view, only the index case showed near one hundred per cent evidence of insulin poisoning with extremely high insulin levels assessed by immunoassay and very low C-peptide levels. In the remaining cases, no insulin or C-peptide data was available, leaving only unexplained hypoglycaemia. The evidence against Norris was largely circumstantial as he was on duty at the time of these deaths, but this is not sufficient by itself to indicate guilt.

At the time, it was believed that such hypoglycaemic episodes, among people who were not diabetic, were "vanishingly rare" (words used by the trial judge), but more recent research has demonstrated that spontaneous hypoglycaemia in sick, elderly, frail patients is not as rare as previously believed.

In any event, Norris has been in prison for over a decade, still protesting his innocence. His case has been the subject of a BBC *Panorama* programme and this year, the official body that examines alleged miscarriages of justice has sent Norris's case back to the court of appeal. The most recent conviction was this year in the USA, when a former nursing assistant was sentenced to life imprisonment for the murder of seven elderly patients at a US military veterans' hospital in West Virginia. Reta Mays murdered them by injecting them with insulin in Clarksburg, producing hypoglycaemia which led to the deaths.

> *"Murder by insulin has been used by a variety of health care workers, including doctors who wanted to conveniently eliminate their wives.*

While the deaths accumulated during her overnight shifts at the hospital in 2017 and 2018, Mays conducted internet searches on female serial killers and watched the Netflix series *Nurses Who Kill*. She pleaded guilty last year in federal court to seven counts of second-degree murder for intentionally injecting the men with unprescribed insulin.

Conclusions
Murder by insulin, although rare, has been used by a variety of health care workers, ranging from nurse serial killers to doctors who want to conveniently eliminate their wives.

Insulin has also been used as a murder weapon in fiction - for any readers who watched *Cardiac Arrest* 25 years ago, series three ended with a psychiatric patient roaming the hospital pretending to be a locum and murdering patients with drug overdoses. He breaks into Liz's room while Andrew is visiting her, and stabs Andrew with a needle containing insulin.

Once called "the perfect crime" due to lack of toxicology evidence, there have been significant advances in analytical chemistry and toxicology since the 1950s. However, proving malicious insulin use continues to be difficult – as highlighted by a 2020 review, entitled 'Is insulin intoxication still the perfect crime?'

Acknowledgements
I am grateful to Professor Vincent Marks for further information on several cases and sharing his presentation to the American Association of Forensic Toxicology in Anaheim in 2020.

References
A full list of references is available on request from the author.

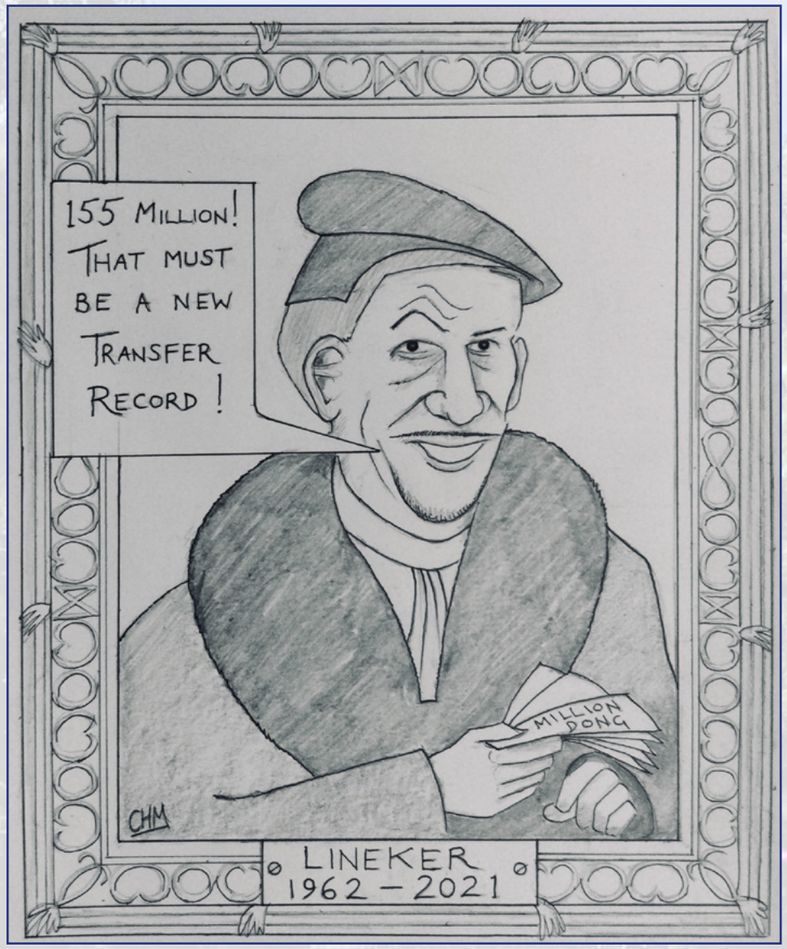
What's in a Name? Farewell Linacre

Dr Steve Ramcharitar
(1993 St Edmund Hall / Linacre College), Interventional Cardiologist at the Great Western Hospital, Swindon

Who or What is Linacre? For many of us, it's an obscure red bricked graduate college that sits at the edge of University Parks. Initially, it was located at St Aldates as an experiment by the University for graduate students when the St Catherine's Society left the historic music building to form an undergraduate college in 1962. Its first fellows included Dorothy Hodgkin (Nobel Laureate) and Sir Isaiah Berlin until it moved to its current location, a former convent in the 1970's. Its proximity to the science block meant it boasted famous Medics/Fellows: Sir Paul Nurse (Nobel Prize Medicine and former President of the Royal Society), Dr Jim Holt, Professor Anthony Bron and in recent years, clinical medical students.

The name Linacre was suggested by Dame Lucy Sutherland, Principal of LMH (1945-71) and the first woman pro-vice-chancellor of the University in recognition of Thomas Linacre (c.1460-1524), a great Renaissance classical scholar, physician and Fellow of All Souls. Some of his early works as one of the first English scholars to study Greek in Italy is exhibited in the college. He pioneered 'new learning' from the great classical texts and amongst his many pupils was Erasmus whose name is synonymous with international scholarships and a Medical School in Rotterdam. Linacre entered Oxford in c.1480, and in 1484, was elected a fellow of All Souls College. Although he did not practice medicine in Oxford, his knowledge, vision and charisma enabled him to become Henry VIII's appointed physician in 1509 before dedicating his later years to priesthood. He pondered on the relationship of Medical Science and God which we all as physicians can relate to. His brilliance we all share as he founded the Royal College of Physicians in London and was its first president. He further aided the RCP by bequeathing to it his own house and library. He also funded two readerships, one at Merton and a lectureship at St John's College, Cambridge. In 1856, Oxford recognised his contribution by establishing the Linacre professorship of anatomy.

The inspiration and legacy that Thomas Linacre set moulded many of its former students. It's not only about the name but the ideology he stood for. But after a half a century, the college is about to change its name which is not without controversy. It has received 155 million pounds from a self-made billionaire Vietnamese businesswoman/philanthropist. It's not the first time financially poorer colleges have changed their name as Manchester College became Harris Manchester after a multi-million pound endowment. Linacre will be the first to completely change to Thao College but hopefully, as medics, we can appreciate what Linacre did for us when we cycle past it on the way to the JR and be inspired.



© Dr Chris Mason (1977 Worcester College)

A Christmas Break

Professor Chris Winearls
(1972 Keble College), Consultant Nephrologist in the Oxford Kidney Unit, 1988 to 2016

A long time ago, I was the duty renal consultant for the Christmas period. The SpR rang to seek authorisation for a patient, who normally dialysed in one of our satellite facilities, to be admitted to the Oxford Renal Ward to allow him to be dialysed in the main central Oxford Dialysis Unit. He had end stage renal failure caused by neglected bladder outflow obstruction caused by carcinoma of the prostate. Now he had severe pain which had worsened since a fall in his bathroom. He could not get into a hospital car and there were no ambulances over Christmas to transport him in a wheelchair to and from his local dialysis unit. He came over and we parked him in a bed. The original pain, he told me, had developed about a month before and he had an X-ray at his local hospital. He had not been told the result. I phoned the DGH – the X-ray had apparently not been reported and was nowhere to be found. We requested another. It showed a metastasis in the neck of the femur. Our orthopaedic colleagues agreed to pin it prophylactically. They asked us to send the X-ray over to their hospital. It never arrived so they could not proceed. I asked for another X-ray. The request was refused on the grounds of unnecessary exposure to radiation. We were told that the first (or should I say second X-ray) would have to be found before he could be seen and operated upon. I knew it was hopeless to expect a search in any of a dozen places between the renal ward in the Churchill and the other hospital site, over Christmas, to be possible or fruitful. I had a mini-tantrum in the doctor's office and decided to try again to resolve matters the next day.

I went in on Christmas Eve to find his bed empty and the juniors beaming.

"He has had his operation." They said, "he was transferred for surgery last night."

"Hooray", but," How," I asked, "was the impasse resolved?"

"He slipped and fell next to his bed and fractured his neck of femur so we got another X-ray and the orthopods were happy to proceed."

He returned to our ward, where I wished him a happy Christmas, but before I could apologise, he thanked me for all we had done for him and said how wonderful all the doctors and nurses were etc. I went home after finishing the ward round and treated myself to an extra slice of lemon in the ginless tonic.

Digital-First Primary Care?

Dr Chris Mason
(1977 Worcester College), Consultant Histopathologist, Exeter

Memories of Oxford Medicine: Part Two

Dr Derek Hockaday
(1947 Brasenose College), retired consultant physician and endocrinologist

The weeks before taking up a consultancy are happy ones. In my euphoria I was persuaded by Jim Hadfield, the Surgical Tutor, to play in the Staff v Students rugby game. I had such a stiff neck after the game that a short West Country holiday with Judith was spoilt, our first ever away from the children.

I soon came down to earth with my first ward round, with a patient who was extremely anaemic from a combination of haemolysis and a hypoplastic marrow. I remembered one of Alec Cooke's aphorisms, 'Never allow death without benefit of steroids', so, we gave her high dose steroids. The response was rapid. She had systemic lupus.

As Peter Sleight used to say, there's nothing so important as reputation, especially if you're applying locally. Three episodes from my pre-consultant time contributed; first, I'd already had a run-in with Alec Cooke, because the system in his Diabetic clinics was for assistants to record their findings, and then for Alec to write the letters to the family doctors on any he wished. I protested that I really was in a better position to describe the state of a patient than he was. He eventually agreed but checked the letters, from which I learned a lot.

Secondly, there was the cricket match, again Staff v Students, at which Paul Beeson, who knew little of the game, was umpire. I lobbied the students for a place against the Staff. Jim Holt, who bowled 'military medium', pitched short on leg stump and I pulled it square threatening Beeson's shins, but he nimbly jumped out of the way. He was one of Pickering's great acquisitions, proving a straightforward, skilful and wisely firm and kind Nuffield Professor of Medicine. He'd been in the American Red Cross medical team that had come to the UK during the War, and had known Pickering then, when he came to review the Oxford option, he was entertained at Ditchley Park, the sky was a perfect April blue. Beeson had the remarkable attribute that if things were going against him in Committee, his 60-year-old eyes would fill with tears, whether under voluntary control or not I never knew. We all had such respect for him, his wishes would be granted.

Thirdly, Pickering ran a highly justifiable campaign to be given a history as the patient had phrased it, however edited in order it might be. After falling below the desired standard, I resorted to what Nero Wolfe's Archie Goodwin described as 'verb-sap', some imagined I expect, until Pickering delivered the immortal words, 'I don't care what the patient said.'

One reason, I fancy, for the rapid ascent of the Oxford Clinical School to surpass those in London was that we were both the secondary referral centre for the Oxford district and tertiary centre for the region. In London, the interest was in the rarer diseases, so the Ambulance Emergency Service was instructed to take many patients with the commoner diseases to the non-teaching hospitals. This meant that clinical research in Oxford often concerned common diseases, such as hypertension, myocardial infarction and diabetes, which was of more use.

This attracted Cambridge students, and then the Oxford pre-clinical ones, usually heading to London. We had smaller numbers of students on each of the five medical and four surgical firms than in London. The students got closer to the patients and the medical staff and had opportunities to perform medical procedures under supervision.

I wasn't a natural Committee person, which saved much time. I couldn't understand some decisions or ways of working. On the Regional Medical Committee, my recommendation of Coronary care units so successfully done in Oxford, was opposed by the regional physicians. Appointment Committees were also instructive. I was on one for a Consultant Psychiatrist. The Chairman, a seemingly decent retired army officer, said to only one of the six candidates 'Before we begin, can I ask if you're a serious candidate for this post?'. She was the only female and had children. Of the two really suitable candidates, one was a good administrator while the other a good clinician. The Committee approved the former. There was also pressure for the recommendation be unanimous. This never made me change my vote. My Committee career in Oxford really ended when on the Medical Board it was claimed that the University was funding more than half the cost of a service. This may have been true of the medically qualified staff, but not I pointed out, the nurses, cleaners, dieticians, etc. My challenge was not in the Minutes but I got them altered.

There are many reasons for research, including the wish to improve care, sheer curiosity, and career advancement, but an important one for me was to obtain more medical help in the Diabetic clinic. In 1966, the average time with a medic for each patient was four and a half minutes. In one way it was an entertaining challenge - could one pick out the patient who really needed help? But it was no way to do things. The NHS was not going to provide more staff, but if one could get a research project approved, and it included the funding for a medic, then it was both very useful, and good for the researcher's career, that he or she do one or two clinical sessions a week. Our research topics ranged widely, often involving the diabetic diet, prompted by two enthusiasts, David Jenkins and Jim Mann. David, who worked in Dan Cunningham's section of the Physiology Department, was developing his 'glycaemic index', a concept to have world-wide impact, while Jim in the Regius' (Richard Doll) department, argued against the high fat content of the traditional 'low carbohydrate' diet, emphasising the importance of the type of fat, particularly its saturation.
The overriding theme was to pay more attention to the food's effect in the body, rather than its chemical analysis on the shelf.

With in-patients, first came a study of the 'insulin-glucose-potassium' regime for patients admitted because of a myocardial infarct. At a British Diabetic Association meeting in Birmingham, I realised that 'diabetic (hyperglycaemic) coma' was being treated in tens of different ways, a sure sign that no one knew what they were doing. Oxford was well placed to tackle the problem. We had George Alberti who had set up a radioimmunoassay for insulin, with two young laboratory assistants, and Hans Krebs' MRC Unit in the RI having been invited there on his retirement from the Whitley Chair of Biochemistry. This meant that we had access to assays for metabolites such as lactate, pyruvate and the two 'ketone bodies'. We could quantitate the 'ketosis', and even more importantly, George showed the plasma insulin levels on conventional treatment to be ludicrously high. We introduced a 'low-dose, frequent' insulin regime, which made mad management easier for hard pressed house physicians.

After Rowan Hillson's help in dispelling the myths surrounding 'chlorpropamide-alcohol flushing', came Sheikh Rashid of Dubai's magnificent gift to fund a research unit thanks in part to Sir Geoffrey Archer, Master of Pembroke College, after his retirement from being the last British Resident to the Trucial Oman states. I was perhaps noticed for curing a Pembroke don of his migraine by recommending a digestive biscuit if he woke during the night. This was based on research which arose from Judith working in the Migraine Clinic. On such details can big funding turn.

The Unit both enhanced and complicated my life. I could employ a personal assistant, Diana Renton, who administered both the Unit and me. The main focus of our work was a prospective study of newly diagnosed T2DM patients to see the relation between their clinical course with standard management and a variety of metabolic and clinical factors. Patients were randomised to two different types of dietary advice. We found glucose levels were more strongly linked to tissue damage than those of any other intermediary metabolite and, along with blood pressure and age, were the key indicators of death or damage. Neither type of dietary advice was clearly superior in this small study of 249 subjects though there was a slight hint that favoured the 'lower fat' diet.

The number of Type 2 diabetics was increasing steadily, as was the number of GPs with some training in their care. The Witney group practice was keen that their diabetic patients be seen there in a joint hospital and GP staffed clinic, and it made sense that one doctor should travel to Witney, rather than 30 patients in the other direction. This idea was adopted in Wantage, Didcot and Bicester, reducing the numbers coming to the JR clinic. Diabetic patients were mainly cared for in their health centres. It is a pity that this transition was not evaluated.

For me, 'On-take' medicine was always fascinating, full of human interest and diagnostic surprise, as was my non-diabetic clinic weighted towards thyroid disease, obesity and what used to be called 'neurotic ill-health'. Help from Senior Registrars became more and more welcome. The precision and scope of tissue imaging was rising rapidly, as was the increasing specialization for referral to others. So, I retired two years early, allowing me to indulge gentle interests, including walking and gardening, labouring in the less polluted country air.

T.D.R.H, 1/5/21

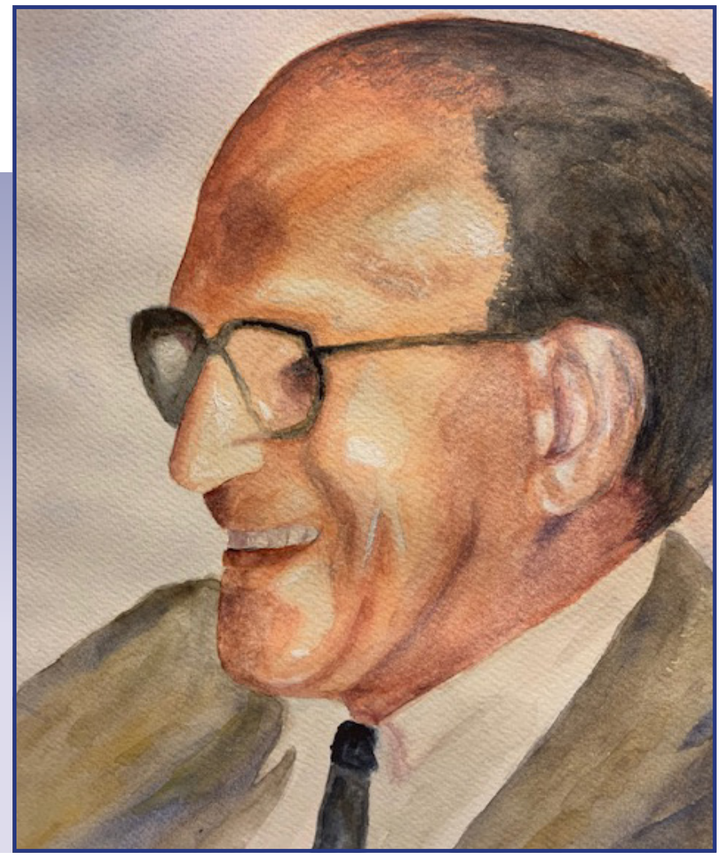
The first part of Derek Hockaday's Memories of Oxford Medicine (1946-66) were featured in the Summer 2021 edition of *Oxford Medicine* (pages 10-11).

www.medsci.ox.ac.uk/get-involved/alumni/publications

A Portrait of Derek Hockaday

Dr Lesley Starr
(1976 St Anne's College), Retired General Practitioner

This watercolour painting is from a photograph of Derek interviewing for the Recollecting Oxford Medicine project. I was hoping to capture his humour and genuine interest in whoever he speaks to.



How Rapidly Time Passes: Four Decades of General Practice in Oxford

Dr Michael Kenworthy-Browne
(1957 Oriel College), retired General Practitioner, University of Oxford

I qualified in December 1964, along with friends Richard Thompson and David Warrell. I started off as house officer to Professor Leslie Witts and five other consultants and then to Professor Philip Alison and Alf Gunning, sometimes working over 100 hours a week.

In 1968, I was the single cardiac registrar in Oxford, with the late Peter Sleight and the late Grant Lee as my bosses; though Brian Gribben and the late Dan Tunstall Pedoe were among the research registrars.

It might have been time to start moving around the country and, even perhaps, to the USA. But with a young family I felt settled in Oxford. So, after an obstetric house job under Professor John Stallworthy, I joined my old College Practice as a GP in July 1970 at 3 Banbury Road, eventually moving to the The Jericho Health Centre at Whitsun 1971 with two other Partnerships. Senator Edward Kennedy, who apparently was interested in health centres, visited us in Oxford in 1972. However, he was far more interested in my identical triplet daughters, then aged six, who had just popped into the surgery, than in the centre!

By 1975, our Practice was responsible for six University colleges, two convents, two Private Halls and the Edward Greene Tutorial College as well as a large city practice, including holding baby clinics around the county. Before long, interested in developing higher professional training for GPs, I became the first Course Organiser for Oxfordshire. This involved developing the two-year rotation for trainee doctors in hospital jobs and persuading consultants to take them on; not always easy. In those days, GP trainees used to be considered second-class doctors, fortunately this is no longer the case. I also had to ensure the quality of the practice for the trainees third year. Some practices had to be turned down.

John Badenoch was my closest mentor in my early GP days. Later on I relied on John Ledingham for more difficult diagnositc problems. I felt, and still do, that a physician's training is the best basis for general practice where being a diagnostician is paramount.

Bent Juel Jenson, the University Medical Officer, asked me to take over a lot of his Oxfam work which required me to study tropical medicine. Bent also asked me to be available, as an emergency doctor, for crises on University territory such as laboratories, libraries and museums but I was only called on about four times a year.

Student healthcare kept me young and, looking after families from the cradle to the grave, was immensely rewarding. Getting to know each patient is a very important part of a GP's life - it can take several consultations to do this.

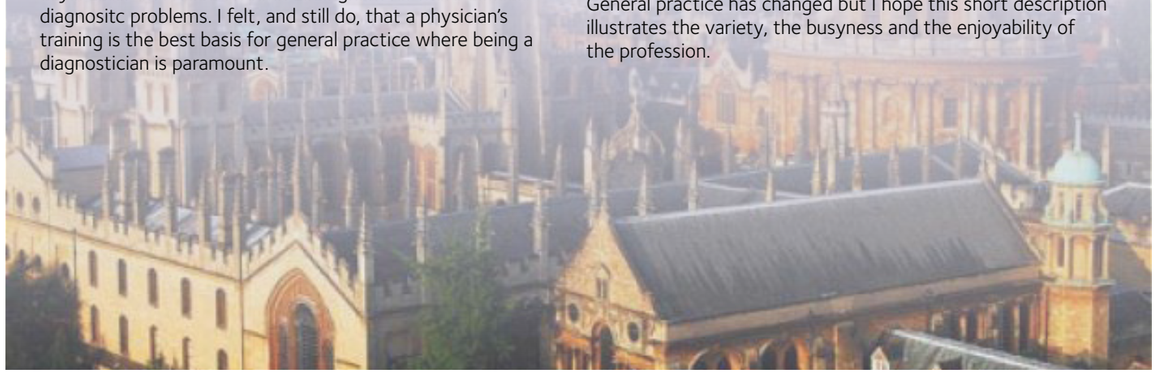
> *"I felt, and still do, that a physician's training is the best basis for general practice where being a diagnostician is paramount*

Kevin, aged 25, came to me during a 'flu epidemic with a high temperature about a week after a urethral dilatation following damage while climbing a fence. Something made me take blood cultures. The following day, I visited him at home and heard a loud heart murmur of mitral incompetence. The laboratory reported that there was no growth, but I sent him into hospital with a diagnosis of acute bacterial endocarditis. The laboratory telephoned two hours later to say that there was beta haemotylic streptococcus on the culture. He was discharged after six weeks parenteral antibiotics and I checked him regularly. He never needed a valve replacement.

I developed a special interest in hypnosis - with some surprising successes. Unusually, I also had a small but faithful number of private patients, which many doctors disapprove of. I had a consulting room and admitting rights to the Acland hospital and would be invited to assist with operations on my patients. And of course, home visits, babies day and night, and visiting patients in the JR.

I worked for the NHS from 1965 to 2001 but stayed on as a private doctor at the Acland and then the Manor Hospital, only retiring in 2011, age 75.

General practice has changed but I hope this short description illustrates the variety, the busyness and the enjoyability of the profession.



Barking Mad

Dr Tim Crossley
(1974 St Edmund Hall), retired London General Practitioner

Dr Kenworthy-Browne, whom I fondly remember from my time as an Oxford region trainee in the 80's, laments the present unpopularity of primary care. I too am flummoxed. What can we do to get a young doctor, let's call him Dr Javid, to commit to it?

Most GPs admit they like the work, but not the job, which means the bureaucracy. Michael's range of patients were in contrast to mine. For instance, driving through Wolverhampton's red light district on call one evening, necessarily at a slow pace, and looking for number three if I could only find it, I admit I was startled to encounter a young woman I knew. Her business offer was hastily retracted when she recognized me. Sex workers are ashamed and rarely admit the work in a consultation but to this day, one of the saddest remarks I ever heard during a long inner-city career was by another troubled woman who said that she had tried being a prostitute 'but I wasn't very good at it'. Like many, she was using street drugs to treat her mental ill health. I wonder if she's still alive.

> *"...if the issue seems simple, they haven't told you everything.*

The inner-city population are diverse, colourful, and exhaustingly poor; at one time I thought that for a doctor who wants to make an impact on the sickest elements of society it was the only place to go. And a GP like me, who started with the homeless in a provincial town and ended up in prison (as a doctor, I may add) can usually top any medical story. But this is wrong, a kind of inverse snobbery which looks down on nominally 'easier' practices in comfortable areas. And I know this from a bruising six-month locum in a middle-class area which I took on towards the end of my career. The assertive middle classes required a very different set of skills, every bit as personally testing as the social war zone I came from.

Patients with their disordered families from whatever income bracket, or patients from loving families, all have complex issues. If the issue seems simple, they haven't told you everything. There is no uniquely physical or uniquely psychological condition, though many patients demur from that idea. And when care is driven by algorithms and mechanics, it gets delegated and over-audited; the primary care physician remains, to make sense of it.

We tolerate uncertainty less now, especially the middle classes. The flood of imaging is seen as a good thing (as if it reduces uncertainty), rather than entrusting our raw clinical skills like listening. In the 1980's, when it seemed to take an act of parliament to get a scan let alone a bed, GPs developed sophisticated risk management techniques that Dr Javid will find scary. But he or she needs confidence in using their own skills and judgement and will find that if they are non-judgmental and interested in people, and then patients, they can carry that risk and be highly effective.

So why is it so hard to get Dr Javid to consider primary care, never mind work where there is a paucity of doctors? After all, the balance of work and life is better now in large measure from the feminising of the profession. Pay is pretty good too....oops....

OK, GPs concerned about pay are generally comparing themselves to their peers in other professions, who may not have the length of training or responsibility they do. Or friends in business or hospital colleagues with healthy private practices. None of whom has the intimate pleasure and reward of long-term family medicine. GPs have to have the confidence not to measure themselves by the money they make. Status drives doctors more than we admit. But perhaps I would say that.

If Dr Javid just wants to get rich, though, there are other options, maybe in the City. In the meanwhile, here is a riddle for non-GP readers; reflecting the decision making in general practice.

What is it that is small, feathered, runs about in a farmyard, lays eggs and barks? Of course, it's a hen. You have to ignore the barking.

We need Dr Javid to throw himself into the exposed, risky and fascinating life Dr Kenworthy-Browne and I have had such luck to experience.

Not All Who Wander Are Lost: Uganda

Dr Nick Wooding
(1984 Oriel College), General Practitioner, Oxford

Mentioning my peripatetic life in medicine to Lyn Williamson at our recent alumni dinner, she quoted the wisdom of Gandalf: 'Not all who wander are lost.' There's a saying in Uganda, where I worked for 10 years, that the person who has never travelled only knows their mother's cooking. Maybe that also applies to those who've never worked outside the NHS. Is there groupthink, everyone swimming together like frogs in the slowly warming pot? Or maybe a better analogy would be the crowds praising the stark-naked emperor's new clothes, not wanting to be the critical voice. After all, whistle blowers' lives aren't easy.

Is that a bit extreme? I remember listening to some discussions at CCG meetings, thinking, 'How did anyone ever think this was a good idea?'

I expected the Ugandan health system not to function. After all, when I arrived in 1997, Uganda ranked among the world's top three most corrupt countries, according to Transparency International. Working for an Anglican mission hospital as medical superintendent freed me from the constraints of the government system; and as a white doctor I could challenge the district administrator's corruption (who wanted the money allocated to some personal project with falsified accounts to accommodate this). I avoided being posted to a secluded government outpost as a punishment for personal integrity, as happened to a friend. He likened it to Shadrach, Meshach and Abednego being thrown into the fiery furnace by King Nebuchadnezzar. But, he said, when you have been into the fiery furnace once, you never get put there again.

So, working in the NHS should be easy; but on reflection it's much, much harder. Who's to blame? The government and the *Daily Mail* with its campaigns to vilify the profession? The BMA, CCGs et al...? Another Ugandan saying states that when you point a finger at someone, you point three back at yourself. How many campaigns have I not voted on, how often have I not written to my MP, instead just concentrating on clinical work without dirtying my hands with the interminable and thankless task of medical politics. This is especially true when we are overworked and burning out, unable to find time to act.

So, responding to Gandalf, here are some reflections from six years in a rural African hospital, four at a Kampala university (including three as Vice Chancellor), and my years as a GP.

1. There's more to life than money. We sometimes choose a lifestyle then fund it through hard work. To be a good doctor, naturally one needs lots of experience. But do we live simply – so that others might simply live (referencing COP26)?

2. No opportunity is wasted: all are stepping stones. I learnt about management and rationing whilst working in resource poor settings. I had little interest in research until I went to a university without a research department so helped set it up. I used that experience to set up research in my surgery. This became an incentive for its takeover when I handed back my GP contract (when last man standing); research was attractive to potential suitors.

3. Quitting is not failure. I once worked for a bully. When I told him I felt he was a bully, he changed (people don't like being called out for bullying). But I still left, for the sake of my mental health.

4. Don't say, 'I am not a committee person.' It's a reason to join committees and challenge any groupthink. People who think outside of the box are vital, even if they make people feel uncomfortable.

5. Take time to develop your spiritual side. Even atheists have faith.

6. Know yourself and your baggage. Myers-Briggs has been an invaluable tool for self-understanding. I once had a dream where I reminisced about telling people exactly what I thought (often in emails). In the dream, someone came to me and told me that they were shocked, since they thought I was a Christian. I realised that I was carrying unresolved anger from the bullying, which I'm now working on. It's important to tell the truth but it must be with love and kindness.

7. No-one says on their death bed, 'I wish I had spent more time in the office.' If you say that, though busy, you give family and friends quality time you are lying to yourself. Quality times follows quantity time.

8. Keep studying. I wish I'd known what I learnt on my MPH as a medical superintendent.

9. Read widely. I've just finished *Black Box Thinking*, and am reading *The Well Gardened Mind* and *Invisible Women*. It's amazing to use what you've read in later consultations.

10. Set a good example. It's hypocritical to give lifestyle advice we don't follow ourselves (especially about exercise and alcohol).

Malawi: Developing Trauma and Orthopaedics in Sub-Saharan Africa

Mr Jim Harrison
(1984 New College), Consultant Trauma and Orthopaedic Surgeon at the Countess of Chester NHS Foundation Trust, in conversation with Mr David Williamson (1974 Corpus Christi College), Consultant Orthopaedic Surgeon

Helping Africans bring African solutions to African problems

How did you come to work in Malawi?
As a Year 5/6 orthopaedic trainee, I heard that Chris Lavy, who'd been my anatomy demonstrator, had gone to Malawi and was working in the main government hospital and the medical school in Queen Elizabeth Hospital, Blantyre. I was approved for a research and clinical post.

What were your reasons for working abroad?
Being a committed Christian was the main reason I went into medicine. I had the sense of being called by God to serve overseas.

How did the children's hospital in Malawi start?
Chris and I were with our children in the park: 'Jim, I've been thinking, why don't we build a specialist kids orthopaedic hospital here in Blantyre because the kids never get a look in – they're always pushed out by the emergencies. Let's make it a Christian Mission Hospital close to the government hospital so that we can teach and train in it.'

How was it funded?
Chris had two contacts: one with Cure International which had a hospital in Kenya and was building a second one in Uganda; and the second was the Beit Trust, a benefactor for Malawi, Zimbabwe and Zambia. They had a centenary and wanted to do a big project. He applied to them to fund the building and to run the hospital. They came and offered Chris the chair of the board and me, the Medical Director post, on the spot. The building happened very quickly – a great contrast to how it would happen in the UK!

How did it develop?
I had input into the building, suggesting some design modifications, and sourcing equipment from various donors around the world. Then there was hiring all the staff. A manager from Cure in Kenya came to work for us. I visited all the District Hospitals in the country to develop systems of referral. Clinics in the District Hospitals were staffed by the orthopaedic clinical officers with me teaching and supervising. After two or three years they didn't need me any longer. The kids only came to the Cure Hospital for their surgery.

Tell us about the research you did in Malawi?
With the high prevalence of childhood bone and joint infections, we were able to publish some important papers on management of these conditions, including an RCT of septic arthritis of the shoulder showing that aspiration was as effective as open drainage. We had a regular UK orthopaedic trainee on rotation. There was a 23 per cent incidence of HIV and we developed protocols for management of fractures in those patients.

How have you continued being involved after returning to the UK?
Just as I was returning to the UK after 11 years in Malawi, I was asked to take over as the Africa Regional Coordinator for the AO Socioeconomic Committee. This has involved coordinating the education of surgeons under the auspices of the College of Surgeons of East, Central and Southern Africa (COSECSA). We set goals on increasing the number of orthopaedic surgeons in each country. It's very important to train surgeons in their own country and for them to remain to work there in the long-term. This was helped by having a COSECSA qualification that was only recognised in Africa.

What further developments have there been?
There are now partnerships of African hospitals with UK Trusts. Trainers go out and train on-site in their partner hospital, again encouraging the local surgeons to stay in their own country. The whole team is now staffed by Africans, and there is no real need for British surgeons to work there long-term, as Chris and I did.

> *"We envision a world where timely and appropriate fracture care is available to everyone*

What other challenges were there?
In various parts of Africa, there are bonesetters and we have seen some terrible complications of their treatments including gangrene requiring amputation. We are working with the governments to provide education to mitigate these practices.

Have you witnessed the effects of climate change?
Yes indeed, for example, there are 800,000 people displaced from their homes by flooding in South Sudan, but this doesn't get into our news.

How do you look back at your time in Africa?
I broke all the rules of advice from people who said, 'Don't do this...and don't do that'. I committed career suicide at every turn, but I believed that this was what I was called to do. Some people have found the return particularly difficult, but by doing what I believed I should be doing, things have worked out. And hopefully I've brought something to the NHS, as well as to Africa.

The Chinese Osler Medical Society
中国奥斯勒研究会

Professor David Cranston
(1983 Wolfson College), Emeritus Associate Professor of Surgery, University of Oxford, and Consultant Urological Surgeon, Oxford University Hospitals Trust

The little village of Batsford in the Cotswolds near Morton-in-Marsh seems an unlikely place for the inauguration of the Chinese Osler Society, yet it was here in 2017 that it happened.

No 1 Batsford

It followed a research link established in 1999 with Chongqing Medical University and the National Ultrasound Research Centre, which led to Oxford having the first Chinese extracorporeal high intensity focused ultrasound (HIFU) in the Western Hemisphere. James Kennedy, now vicar of St Mary's Church Chipping Norton, was the first HIFU surgical research fellow and through his DPhil research on liver and kidney cancers, was responsible through those clinical trials in obtaining the CE mark on the JC Haifu machine.

High-intensity focused ultrasound can be likened to a magnifying glass focusing the sun's rays onto the back of one's hand causing a burn. Increasing the power of ultrasound 10,000 times allows penetration through the skin into the body focusing the energy to a point the size of a grain of rice at 70 - 80°C causing immediate destruction of tissue.

It was on my first visit to the research centre in China in 1999 that I was amazed to see a large picture of William Osler on the wall with a quote reputed to be from him saying:

"Diseases that harm require treatments that harm less".

And it is certainly true that the scientists and physicians that I have got to know over the years in China have a very holistic and humanitarian approach to medicine which is very encouraging given what often appears today in the media. Thus, it was in 2017 we hosted a visit of 12 senior Chinese physicians and surgeons to Oxford. They included Professor Zhang Yanling, then President of the Chinese Medical

JC Haifu machine

Association, responsible for three million doctors in China, and Professor Lang, Emeritus President of the 200,000 members of the Chinese Association of Obstetricians and Gynaecologists. A tour of the Cotswolds finished with tea at my son's rented house in Batsford village and the Osler Society of China began.

High intensity focused ultrasound is a non-invasive technology allowing ablation of tumours deep within the body. More information on this is available on the Voices from Oxford website: **www.voicesfromoxford.org/using-ultrasound-to-treat-cancer**

Tori Kennedy demonstrating how to eat scones to Professor Zhang

Professors Zhang and Lang in Osler House

Critics Corner: OMLC Lecture Series

Dr Sarah Ball
((1974 Somerville College), Conservation Geneticist and retired Consultant Paediatric Haematologist

'Exciting Progress with Malaria Vaccination'
Monday 26 July 2021
Sir Adrian Hill, Lakshmi Mittal and Family Professorship of Vaccinology; Director of the Jenner Institute; Co-Director of the Oxford Martin Programme

Eavesdropping on the Clapham omnibus might suggest that we are all vaccinology experts now, and that generating an effective vaccine is simple and the working taking months rather than years. However, quietly in the background, starting long before and continuing throughout the heralded Covid vaccine breakthroughs, the development of an effective malaria vaccine has been taking place. The pathway to this Oxford-developed vaccine has involved an impressive degree of cooperation between many disciplines, including the delivery of a phase 2b vaccine trial in Burkina Faso, as well as the rivers of patience essential to reach such a long-term goal. Fascinating and informative, the talk provoked many questions from both live and Zoom audiences, which included many NDM or infectious disease stalwarts familiar with the progress of the project over the years. For example, might the immunisation of such young children impede their acquisition of natural immunity, potentially counteracting the early benefit of the vaccine? And how might this help to answer the long-standing question of the population protection against malaria associated with haemoglobinopathies, itself the subject of Professor Hill's doctoral research.

'Immunity to Viral Infections'
Monday 27 September 2021
Professor Paul Klenerman, Sidney Truelove Professor of Gastroenterology
bit.ly/OMA-Klenerman

Professor Klenerman treated us to an erudite overview of the different components of the immune response to viruses, including Covid-19, and how this has been investigated in patients. Of particular interest was the discussion of the balance between immunity and immune pathology, and more coverage of the pathways associated with triggering of coagulopathy would have been very welcome. Occasionally, the sheer number of acronyms and the level of detail contained within some of the slides, felt a little daunting, but that did not detract from what was an otherwise excellent and informative talk. As with other Covid-related subjects, this has very much been a team event, as shown by two slides packed with details of different laboratories and personnel involved in this wonderful example of cross-laboratory collaboration.

'Virtual Reality for Mental Health Disorders'
Monday 25 October 2021
Professor Daniel Freeman, Oxford Professor of Clinical Psychology
bit.ly/OMAFreeman

This was a fascinating talk, lavishly illustrated with videos of virtual reality (VR) scenarios, on the power of VR cognitive therapy in the treatment of phobias, with the potential for enhancing treatment options for patients without easy real-life access to specialist psychology. In the ongoing gameChange trial, this approach is also being evaluated in patients with psychosis. The rationale is that cognitively controlled exposure to even rudimentary VR scenarios, can generate "counteractive memory", which can override fearful memories associated with trigger situations. In one illustration, we were shown that VR cognitive therapy can allow a sufferer of severe acrophobia to step onto a (virtual) high narrow ledge to rescue a (virtual) cat from a tree. Professor Freeman's catastrophic (geddit?) joke may have fallen a bit flat (sorry), this being his first face-to-face lecture since the first Covid-19 lockdown. But no more fear of falling; this was 'brainwashing' with impeccable style by a very impressive, entertaining, and articulate speaker.

'How not to make a bad thing worse - rethinking psychological trauma'
Monday 29 November 2021
Professor Sir Simon Wessely, Regius Professor of Psychiatry, Institute of Psychiatry, King's College London

Another impressive, entertaining and thought-provoking talk given by another distinguished and decorated Oxford alumnus. Many of the take-home messages were simple and intuitive - don't panic, provide practical support, facilitate contact with family and normal support network. But to reduce the risk of PTSD, don't jump straight in with on-the-spot counselling in the immediate aftermath of a trauma (which made me wonder, has anyone measured the effect of the Prime Minister appearing at the hospital bedside of victims?) The relaxed, off-the-cuff delivery with invited audience participation should not belie the seriousness and depth of the substance of the talk. For those who were interested, it was agreed not to go into any detail of the speaker's appearance on Desert Island Discs earlier this year.

Details of previous and forthcoming lectures can be found here: **www.medsci.ox.ac.uk/get-involved/alumni/events-and-reunions/oxford-medical-lecture-club**

Recollecting Oxford Medicine: Part One Complete

Dr Derek Hockaday *(1947 Brasenose College), retired consultant physician and endocrinologist, and* **Dr Peggy Frith**, *New College Dean of Degrees*

Two things stand out from these interviews. Pre-clinically, the revelation by the undergraduates, echoed by their tutors, that they should think for themselves. So, it's not what you've been taught to believe, it's not what everyone else is saying, but it's what you consider the best explanation of the facts placed before you with proper enquiry as to how those 'facts' were obtained. And that approach was not totally abandoned clinically; when presented with the maxim 'When you see a bird flying past the window, it's more likely to be a sparrow than a heron', one was allowed to reply, 'And when you see a heron flying past the window, it's more likely to be a heron than a sparrow'. Observation and discrimination were ranked high.

Secondly, how very many people worked long and hard to make the Oxford hospitals a better place for patients and so a better place to learn clinical medicine. As these interviews show, different people had different tactics, but this strategic aim was widely accepted and widely applied. The School was never more successful than when the University and NHS staff had an equivalence, though not sameness, that led to harmonious collaboration.

A year later, we're happy to report that the number of interviews available has risen from 18 to around 50. The detailed work of assembling the podcasts has mostly been most ably done by the Bodleian's Kelly Burchmore, all made possible by a most generous anonymous donation negotiated by Dr Peggy Frith.

A further task is to make available the three interviews available only as transcripts: Mr Malcolm Gough; Prof Ken Fleming; Prof Michael Gelder. And we're not done yet: this is an on-going project, with three new interviewers recently recruited.


Mr David Tibbs


Prof David Warrell


Prof Derek Jewell


Dr Donald Lane


Prof George Alberti


Prof Godfrey Fowler OBE


Dr Grant Lee


Mr Hung Cheng


Dr Hywel Jones


Dr Trevor Hughes


Dr Jim Holt


Dr Joan Trowell


Mr Joe Smith OBE


Prof John Ledingham


Mr Andrew Freeland


Mr Chris Adams


Prof Chris Redman


Dr John Oxbury


Prof John Spalding


Mr Julian Britton


Prof Chris Winearls


Sir Christopher Paine


Prof David Paterson


Prof Keith Hawton CBE


Dr Michael Tunbridge


Mr Mike Gillmer


Prof Neil Mortensen


Mr Nick Dudley


Dr Peggy Frith


Mr Peter Burge


Prof Peter Sleight


Prof Pierre Foex


Prof Richard Boyd


Prof Richard Moxon


Dr Robert Twycross


Dr Sue Burge


Prof Terence Ryan


Prof Tony Hope

Missing Photo: Brian Longworth


Mr Michael Dunnill


Mr Malcolm Gough


Mr Ken Fleming

CLICK ON THIS LINK TO LISTEN TO THE PODCASTS:
https://podcasts.ox.ac.uk/series/recollecting-oxford-medicine-oral-histories

2021 Reunions

We are very pleased to have held in-person events for this year's anniversary reunions, as well as rescheduled celebrations from last year, postponed due to the Covid-19 pandemic. Events were held at Balliol College, Trinity College, St Hilda's College, Magdalen College and Pembroke College. It was wonderful to see so many alumni and we hope you enjoyed reminiscing with old friends. We look forward to seeing more alumni at next year's reunion events, details of which will be sent by email. If you would like to be a champion for your cohort, please email Bella Pratt, Alumni Relations Manager, at oma@medsci.ox.ac.uk. Below are a few reunion photographs from this year.


1981 Graduates, Balliol College, Saturday 31 July 2021


1990 Graduates, Trinity College, Saturday 30 October 2021


2010 and 2011 Graduates, St Hilda's College, Saturday 07 August 2021 ©Sally Young


2000 and 2001 Graduates, Pembroke College, Saturday 02 October 2021

Obituaries

DR RICHARD GREENHALL (1943 - 2021)

Professor Charles Warlow, Neurologist, and Professor Kevin Talbot (1994 Exeter College), Head of the Nuffield Department of Clinical Neurosciences and Professor of Motor Neuron Biology.

Dr Richard Greenhall devoted the whole of his professional life as a neurologist to working exclusively in the NHS. Never one for pushing himself forward, he was the sort of full-time consultant who provides the rock on which the NHS stands, totally dedicated to his clinical service and to his patients.

Richard was a Birmingham boy of Welsh heritage who after leaving King Edward's School went up to Cambridge in 1962, initially to read natural sciences, although he soon switched to medicine. After clinical training at St Thomas' Hospital in London, and junior hospital doctor posts in Oxford, Bristol, and London, he started training in neurology under Bryan Matthews in Oxford. Completing his DM thesis in 1975, he flirted with the idea of becoming a neuropathologist, but decided to continue his training as a neurologist. He was appointed senior registrar at the National Hospital for Neurology and Neurosurgery, Queen Square, and St Mary's Hospital in London, an unusual move when at the time almost all the Queen Square senior registrars had previously trained at the National Hospital.

In 1977, he was appointed consultant neurologist in Oxford and Reading, exchanging Reading for Aylesbury three years later. He served on the council and the services subcommittee of the Association of British Neurologists and as regional specialty adviser at Swindon & Marlborough NHS Trust. For neurology he helped: develop the neurology services in Oxford and surrounding district general hospitals; was behind the introduction in Oxford of nurse practitioners in Parkinson's disease and epilepsy; and was sought after as an expert witness in medicolegal cases. Several generations of neurologists trained in Oxford and beyond have cause to be grateful to Richard for his kindness, and for his influence as a teacher and clinician. He wore his knowledge lightly and was completely lacking in pretentiousness. Even the most junior neurology trainees felt valued and were put at their ease and made to feel an important part of the team. Regular Friday after work debriefing sessions at the Royal Oak across the road from the old Radcliffe Infirmary (obligingly facilitated by the hospital switchboard operator with a pager message to attend meeting on "Oak Ward") were an opportunity to benefit from the wider curriculum of cricket, music, politics, and neurological gossip. Richard had an unwavering commitment to the NHS; he always put patients first, and was never particularly motivated by seeing his name in print although he could hardly object to neuropathologists still referring to the "Greenhall" line when assessing cerebral swelling, one product of his DM research. Although he shunned the limelight, sat at the back of lecture theatres, and only rarely asked a question, he was very much sought after as a medical student teacher, as well as for careers advice by many generations of neurology trainees who always felt much supported. In a career of more than 30 years he published only a handful of papers in his own name, while always championing and supporting the efforts of his academic colleagues. His positive influence on the culture of Oxford neurology is a far greater and lasting legacy.

In retirement he was able to spend more time with his family, reading the Guardian and Private Eye thoroughly, listening to the wireless (never the radio), watching rugby at the Millennium Stadium, football at The Hawthorns, and cricket at Edgbaston, taking unusual train journeys, and chopping wood in his beloved cottage in Wales. He leaves his wife, Elizabeth, whom he met when they were at school in Birmingham; their children, Owen, George, and Ruth; and five grandchildren.

Taken from the *British Medical Journal*, published 30 July 2021: **www.bmj.com/content/374/bmj.n1892.full**

PROFESSOR GEORGE ROBERT FRASER (1932 – 2020)

Mrs Maria Fraser

Professor George Fraser (1957 Green Templeton College) is a pioneer in many fields of human genetics who throughout a long and active career, contributed to the understanding of the diversity of the human genome. He has made major contributions to clinical genetics, to the delineation of syndromes (including Fraser syndrome), to the amelioration of inherited disabilities of hearing and sight and overall, to the refinement of methods for linkage analysis and fundamental population genetics.

George Fraser, a Winchester Open Scholar, graduated in medicine from Cambridge in 1956. After his PhD thesis with Professor L S Penrose in London in 1960, he held academic appointments in England, the USA, Canada, Australia and the Netherlands before returning to work in Oxford in 1984. It is here that he established the first clinic in familial cancer of breast, ovary and colon under the aegis of Walter Bodmer, Director of ICRF. The clinic since then is flourishing and goes from strength to strength.

George's name is inextricably linked to Pendred syndrome (Fraser 1959). Fraser's systematic studies crystallised the variable penetrant that is the hallmark of Pendred syndrome and brought the disorder to the attention of a wider public. His data categorically establish the autosomal recessive nature of the syndrome and enabled a prevalence figure of 7.5 per cent of all childhood deafness (Fraser 1965) to be estimated.

George has made important contributions to the genetics of blindness (Fraser and Friedman 1967- a book which represents a revised version of the MD thesis presented to the University of Cambridge for which he awarded the Raymond Horton-Smith price for the best MD thesis of the academic year 1965-6).

George made a very significant contribution to drafting the first edition of McKusick's indispensable catalogue, Mendelian Inheritance in Man (McKusick 1966).

George has been linked eponymously to the Fraser syndrome, a rare autosomal recessive disorder characterised by a multisystem malformation usually comprising of cryptopthalmos, syndactyly and renal defects. George alluded to two sibships he had seen with this condition in the context of considering the role of autosomal recessive inheritance in congenital malformation (Fraser 1962). Subsequent reports have linked his name eponymously with the condition (Gorlin 1990).

George's contributions stand the test of time. His own observation and subsequent action of one such sufferer of Fraser syndrome at the age of five years reveals George's noble nature. When he first met the blind and deaf child she was only screaming and behaving like a wild animal. He noticed that she liked to press ticking clocks to her skull and, suspecting that her deafness was largely conductive he took her to an otorhinolaryngologist of his own acquaintance who reconstructed the malformed middle ear ossicles and at the age of six years, she heard speech for the first time; more than four decades later, she lives a life more tolerable than it would have been without hearing! In his own words George believed that his small contribution to the improvement in the quality of life of this girl represents a greater achievement in his life than that of his name becoming attached to a syndrome, or even, in abbreviated form as FRAS1, to a gene, whether in Man or in the mouse in which homologous genes have been studied, or in any other living creature. Following the sequencing of the human genome the discovery of the genes responsible for the Fraser syndrome have been identified.

In Memoriam

Professor Frederick Fastier *(1948 Balliol College)*
died 23 July 2021

Dr Robert Adriaan Pieter Kark *(1959 St John's College)*
died 15 June 2021

Mr Nigel Hawkes *(1962 St Catherine's College)*
died 06 October 2021

Dr George MacPherson *(1960 Oriel College)*
died 14 November 2021

Dr John Pittard *(1969 Magdalen College)*
died 23 March 2021

Dr Beatrix Ruckli *(2002 Kellogg College)*
died 08 September 2021

Please contact the OMA team (oma@medsci.ox.ac.uk) regarding any obituaries of friends or colleagues you would like to be considered for entry into the next edition of *Oxford Medicine*.

NEWS & CONGRATULATIONS

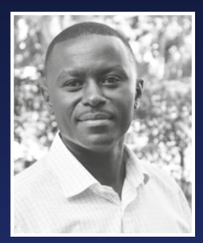
PROFESSOR SIR PETER HORBY, Professor of Emerging Infectious Diseases and Global Health, has been awarded the prestigious Alwyn Smith Prize for 2020/2021 by the Faculty of Public Health in recognition of his outstanding service to public health as a global leader in epidemic science.

PROFESSOR SIR JOHN BELL, Regius Professor of Medicine, has been selected for induction into the Canadian Medical Hall of Fame, for his pioneering advances in the era of translation research, bringing ground-breaking laboratory discoveries into the world of practical medicine.

PROFESSOR TRISH GREENHALGH, Professor of Primary Care Health Sciences, was Highly Commended in the O²RB Excellence in Impact Awards 2021 for her significant contribution to policy discussions and public understanding of Covid-19 precautions internatonally.

PROFESSOR JOHN ANDREW TODD, Professor of Precision Medicine and Director of the Wellcome Centre for Human Genetics and of the JDRF/ Wellcome Diabetes and Inflammation Laboratory (DIL), has been awarded the 2021 EASD-Novo Nordisk Foundation Prize for Excellence for his decades of effort to understand, prevent and combat type 1 diabetes.

PROFESSOR SIR PETER DONNELLY (DPhil Mathematics, 1980 Balliol College) has been presented with the Gabor Medal by the Royal Society for his pioneering work in the genomic revolution in human disease research, transforming the understanding of meiotic recombination, and for developing new statistical methods.



PROFESSOR GEORGE WARIMWE has been awarded The Royal Society Africa Prize for his work on zoonoses vaccine development, capacity building in Africa, and his innovative research proposal. He is currently working on viral infections that are transmitted between humans and animals in Africa with a focus on vaccine development for their control.

DR TANMAY BHARAT (2006 Hertford College), a group leader at the Sir William Dunn School of Pathology, has been awarded a prestigious Lister Institute Research Prize in the 2021 funding round.

DR ALEXANDER (SANDY) DOUGLAS (2004 New College), an investigator at the Jenner Institute, Nuffield Department of Medicine, has recently received two prestigious Wellcome accolades. Dr Douglas was awarded a five-year Wellcome Stage 2 Clinical Research Career Development Fellowship, receiving £1.3m of funding to investigate development of new vaccines against rabies and Epstein Barr virus. On the back of his strong fellowship application, he also was one of four recipients of a Wellcome-Beit prize, worth another £25k of funding. This prize is awarded annually to Wellcome's strongest applicants across their range of intermediate-level clinical & non-clinical fellowship schemes.

PROFESSOR ALISON SIMMONS, the Director of the Oxford University MRC Human Immunology Unit (MRC HIU), together with **DR HASHEM KOOHY**, group leader at Radcliffe Department of Medicine and the MRC HIU, have been awarded a Chan Zuckerberg Initiative Paediatric Networks for the Human Cell Atlas grant.

Medical School News: Resilience, Kindness, Professionalism....Oh My!

Dr Catherine Swales
(1997 Wadham College), Director of Clinical Studies, Oxford

"When will it end?" ... If I'd got a pound for every time I've heard that phrase about Covid I could build a new education centre, buy a yacht and sail off to retirement in the Maldives. Well, not quite – but not far off. And if it's not Covid directly, it's the knock-on effect of an NHS (and therefore its staff) that is creaking at the seams. Everyone is digging deep - braced for the winter and thereafter still a long haul. Under these circumstances, those elusive qualities that mean so much in students, trainees and seniors fall under pressure: kindness, resilience and professionalism. When there's little resource left, those traits run the risk of being the first to go. Conversations become less rich and more transactional, energy levels become depleted, leading to vulnerability and isolation - and tempers fray. That said, I'm constantly amazed by my friends and colleagues (and those who were colleagues but are now friends!) and their sense of grit, of doing the job right no matter what, and still pausing to smile, to comfort and to sustain those around them. That seam of strength should certainly not be taken for granted by Government however, but I think that's a topic for another day...

So where does it all come from? Can you spot resilience at interview? Is it possible to teach kindness? How on earth do you assess professionalism? It is to be fervently hoped that most sixth formers have not had to demonstrate significant resilience so early on in their lives (although alas some do, and show extraordinary strength), and as a result there's little 'pilot data' for them to be able to call on, or for interviewers to test. That said, the Oxford interview in itself might be arguably a test of resilience – but so much changes over the time between interview and arriving, and arriving and graduating. A lot of water flows under the bridge in those few years, and some of it is troubled. Our welfare teams in both preclinical and clinical are acutely aware of this and are focusing attention on helping students to learn these skills, so that they have the internal resources to lean on when the going gets tough. For many – indeed for most – that's all they need. Our students by and large not only pace themselves, but excel in so many ways, though it would be arrogant and foolish not to recognise that for a few the pinchpoints are very profound indeed. For those there is a fine line between helping them to manage and seeing when they can't – and helping them to see that too. There is nothing to be gained from just keeping going, to reach a finish line that is only actually a start line for a new set of challenges, with different (and sometimes fewer) mechanisms of support. A break, a pause for breath, to retreat, regroup and return can make all the difference in the world.

And what of kindness? For all their work on Outcomes for Graduates, in which the GMC have put professionalism front and centre, there is no mention of kindness. Not one. And yet I suspect it's often what patients seek most. Inherent in kindness is the understanding that we are not alone, and that others have battles often greater than ours; it can also be one of the most powerful agents for change - but it's not a curricular requirement. Aesop said, "No act of kindness, no matter how small, is ever wasted", and whilst I accept, I am more than a little biased (ahem), I believe our students understand that, and are that – to each other, themselves, and the people around them.

> *"Can you spot resilience at interview? Is it possible to teach kindness? How on earth do you assess professionalism?*

As for professionalism? Well, that remains an important area for all Schools to develop in teaching and assessment, and one with which we are all grappling. Examining it in a meaningful way is more longitudinal (and therefore complex) than 'simply' incorporating into an OSCE or reflective pieces – and the latter are only as valuable as the thought that goes into them. How does one examine an *identity*? I accept that the Situational Judgment Test tries to achieve that as part of the Foundation application process, but a recent SJT revision session with the Final years provoked such a vibrant discussion about even the most 'obvious' case, I wonder if ranking, rating and selecting responses can really test it in any meaningful way. Research into this area abounds of course – but the value of that also depends on which metric matters, and which gets picked ... and has anyone asked the patients what they prioritise most?

That's all from me for now, except to say good luck and good thoughts to our Finalists as they make their way through an undoubted pressure point in the year: 2nd BM exams, job applications and SJT – all squashed into a few short months. A test of resilience indeed. I wish them well and am so proud of them.

Climate Crisis = Health Crisis: Medics Sound the Alarm

Chloe Freeman *(2020 Somerville College)*, **Hannah Chase** *(2018 Green Templeton College)*, and **Roshan Karthikappallil** *(2018 University College / Green Templeton College)*

Building on the Summer edition introducing Education for Sustainable Healthcare (ESH), medical students Hannah Chase, Chloe Freeman and Roshan Karthikappallil share updates, experiences, and climate facts.

COP26. A pivotal moment of climate negotiations disappointingly culminated in an anaemic agreement - global leaders lacked the courage to steer the world from climate catastrophe. If you only watch one speech, the powerful words of Barbados PM Mia Mottley reminded us that *"We exist now …we want to exist 100 years from now"*.

Medical Sciences Division (MSD) Declares a Climate Emergency

In October, after six months of campaigning led by Roshan, Oxford MSD signed a joint declaration stating the climate and ecological emergency is a health emergency, alongside many medical schools. Despite this huge leap forward, it is disappointing that making the statement publicly available - the definition of a declaration - is not a priority from the MSD. It must be, alongside aligned commitments.

ESH Progress Within the Medical School

Planetary Health has been further incorporated into many curricular threads, including a new Special Study Theme in Planetary Health and Sustainable Healthcare offered in fourth year. This allows students to dive deeply into the reality of climate and health. As medical professionals, we have a unique responsibility to prevent a devastating public health crisis, requiring the medical school to prepare us accordingly.

Secondly, an ESH faculty lead post has been created. This position is a clear statement of commitment from the medical school, and we are delighted that Dr SanYuMay Tun has accepted the position to build on previous work and will be starting in December.

Healthcare Workers Take to the Streets

Alongside COP26, Saturday 06 November 2021 was a Global Day of Action for Climate Justice with marches around the world in support of system change for a just transition. In Oxford, medical students, diverse members of the Oxford healthcare community, and MSD faculty formed a vibrant health bloc. The positive public response to the Oxford NHS staff and students' presence at the march was uplifting and proved the quote that 'Hope is more the consequence of action than its cause.' Surrounded by colleagues, with a shared sense of urgency, a rainbow appeared over Broad Street - a fitting symbol of hope.

Health Professionals at COP - a Medical Student's Lens by Chloe Freeman

"I felt it important to be in Glasgow during COP26. As a student, I feel it's imperative to inform myself of the impacts of climate change on people and planet and how it is shaping the practice of medicine. Although labelled the most exclusive COP yet, the Health Pavilion signified the necessity of including health within negotiations. However, the truth is I still feel sceptical about the real systemic change we need to see.

Despite this, alongside the conference, COP26 Coalition People's Summit was an incredible four days of listening and learning. Stories were shared by those living with a daily reality of climate change, and flickers of hope allowed me to envisage a future where climate and social justice are realised. In Glasgow, a rainbow also appeared during the march, a reminder of our shared struggle. We have the solutions, we have creativity, now world leaders need to listen."

Reality Check

» Air pollution kills 8.7 million people per year. In Oxford[1] alone, higher pollution days are linked to six cardiac arrests outside hospital and eight strokes per year. Healthier modes of travel simultaneously protect our climate, bodies and minds.

» A third of all greenhouse gas emissions come from food production. Red meat has the biggest contribution.[2] The average UK citizen eats 88kg meat/year. A diet to save our planet must include a maximum of 25kg/yr including only 5kg of red meat and pork. Furthermore, we know it drastically reduces all-cause mortality. Hospital catering needs to up its game – ideally adopting the Planetary Health diet.[3] Both financially beneficial and improving patient health outcomes.

» The NHS, responsible for five per cent of UK emissions, are committed to Net-Zero by 2040. Are the workforce prepared? No. Does OUH have a Green Plan after failing to produce a Sustainability Development Management Plan by March 2020? No. We are beyond needing to make incremental changes or 'blah blah blah'. Emissions must be cut in the next decade for it to make a difference to the youth of today.

How about individual healthcare professional responsibility in all this? Translate eco-anxiety into practical action… Challenge systemic structures, lobby your trusts and personal choices. If you would like to inform yourselves and your patients more, this RSM webinar series is an excellent introduction: **www.rsm.ac.uk/latest-news/2021/climate-change-series-resources-on-health-and-climate-change**

References

[1] www.cleanairfund.org/publication/policy-brief-oxford

[2] ourworldindata.org/food-choice-vs-eating-local?country

[3] eatforum.org/learn-and-discover/the-planetary-health-diet

Pre-Clinical School News

Professor Robert Wilkins *(1990 St Catherine's College), Director of Pre-Clinical Studies, Course Director of the Biomedical Sciences Programme, Associate Professor in the Department of Physiology, Anatomy and Genetics, and Tutorial Fellow at St Edmund Hall*

After four pandemic-disrupted terms - with recorded lectures and the odd distanced practical class run for groups of 15 - I am delighted to report that the pre-clinical course has returned to in-person teaching. While the requirement to wear face coverings within teaching spaces remains, in all other respects, the term has proceeded along very similar lines to Michaelmas 2019. Fingers are crossed that the remainder of the academic year will proceed as smoothly and that examinations, which for the last two summers have had to be conducted using modified online approaches, can return to their normal formats.

One consequence of the need to deliver teaching through online platforms was the rapid acquisition of 'lecture capture' technology in our teaching spaces, enabling the streaming and recording of lectures and seminars. In pre-pandemic times, student representatives had been advocating for lecture capture and I know they are grateful that this technology is now in place, giving students an electronic resource for each teaching session that they can review at leisure.

One aspect of teaching that has remained online has been the delivery of anatomy teaching, but not for pandemic reasons. Revised regulations governing safe levels of formaldehyde in the anatomy suite in the MSTC delayed the reintroduction of hands-on anatomy classes while downdraft tables and other mitigating measures were installed. I am delighted that this is now complete and pre-clinical students will resume in-person anatomy classes before the end of the term.

Finally, I would like to pay tribute to Dr Laurence Leaver (1988 Green Templeton College), who stepped down this summer after four years as Associate Director of Pre-clinical Studies (Health and Welfare). During that time, Laurence helped many students navigate the pre-clinical course and I know they have appreciated his kindness and sound counsel. As Laurence's successor, we welcome Professor Kate Saunders, whose role has been expanded to include curriculum development as it applies to student well-being.

Alice's Adventures in Pre-Clinical Medicine

Alice McGonnell *(2019 New College)*

The phrase "full-on" best summarises my experience of preclinical medicine. When I first arrived, I was determined not to miss out on any experiences so I joined the University Equestrian Club, the College Rowing Club, and both the College and Millennium orchestras. Alongside these was the shock of having a syllabus thicker than my bedside novel handed to me. How was I ever going to know all this?! Who knew there was so much to know about aquaporins! Prosection was a highlight of my first year. After a (usually rather heavy) Wednesday sports night out, there was nothing like the smell of formaldehyde and the sight of preserved flesh to wake me up.

Sadly, cosy tutorials and prosection sessions ended when Covid-19 hit, and online learning arrived. The only bonus was our exams were postponed! However, when second year arrived, we were sent back to college. College felt more like a prison: no sport, no Evensong, no formal dinners and no bops. With nowhere to go and nothing else to do, Michaelmas 2020 was largely spent staring at a screen battling a crippling workload.

After another term at home and a major set of exams, Trinity 2021 felt like a blessing. Competitive sport was back along with Evensong and formal dinners. We made up for lost experiences with a late Halfway Hall and various inter-college sports competitions. Third-year work began, and we were able to choose topics of specific interest. Essay-writing was no longer a chore, and I particularly loved discussing the physiology of spacetravel in a tutorial. I was lucky enough to represent the University in a student horse race at the Curragh Racecourse in Ireland, and I have taken up modern pentathlon, making some fantastic friends. In contrast to library sessions and essay crises, I have been carrying out a research project at OCDEM, gaining an insight into how scientific research is performed. Next term, I head back to the library to prepare for final exams before clinical school commences. As preclinical medicine draws to a close, I cannot wait to spend more time in the hospital and start feeling more like a proper doctor!

Osler House News

Carolina Valensise
(2013 Pembroke College), Osler House President

This September's annual Fresher's Dinner celebrated the introduction of fourth- and second-year graduate-entry medics into Osler House. The opportunity to dine in St Edmund Hall amongst the new clinical intake finally reintroduced a sense of normality to life as an Oxford medic. As Covid-19 withheld this opportunity from my own peer group, it was truly a pleasure to see so many medics beaming with joy and excitement after such a difficult 18 months. Fresher's Fortnight (brilliantly organised by the previous Osler Committee) also celebrated the start of the new academic year with a scavenger hunt across Oxford, a 'meet the Osler parents' evening and of course, the return of the infamous Osler Bop! Additionally, Osler House itself has been re-opened, allowing students to say goodbye (somewhat...) to dreaded zoom teaching sessions and relax with peers after a long day at the JR.

One of our biggest priorities entering the new academic year has been student welfare. Welfare drop-ins and posters highlighting points of contact within the medical school have been set up to ensure ongoing support for all clinical students. We are also aiming to re-establish the peer support network within Osler House. This will give students access to peer-to-peer listening services which aim to provide a less formal point of contact for welfare issues. Alongside these initiatives, Osler House has been lucky enough to put on two bops this term, allowing for increased social integration both within and between peer groups.

Our LGBTQ+ reps, Desson and Charlotte, have taken charge of welcoming all LGBTQ+ medics and allies into the Osler community. A fantastic drinks evening at the Jolly Farmers attracted students across all year groups and the duo have plans to run similar events throughout the year. Sports at Osler are thriving this year, with the popular 'casual kickabouts' taking the clinical school by storm. Open to all, these relaxed afternoon sessions allow students to let off some steam and have also highlighted the footballing talent at Osler House, a promising sign for the annual Varsity Sports Competition against Cambridge to be held in Hilary term!

In other sporting news, Osler House Boat Club has flourished into one of the most successful boat clubs in Oxford. Impressively, both crews gained blades in the most recent Summer Torpids and the Club completed an immense row from Oxford to London in November to raise money for the Tingewick charities and a new boat! We are all incredibly excited to see what this year has in store for the Club. All in all, Osler House is back and better than ever!

Tingewick is Back

Meirian Evans *(2017 St Catherine's College)* and **Charlotte Rose** *(2017, Magdalen College)*

What a year! Joining both clinical school and the Tingewick Society mid-lockdown made the start of the year a busy time for the 30 medical students who make up Tingewick Firm. Our challenge was huge in 2021, when the fifth years hadn't been able to experience a pantomime as fourth years before taking over the society.

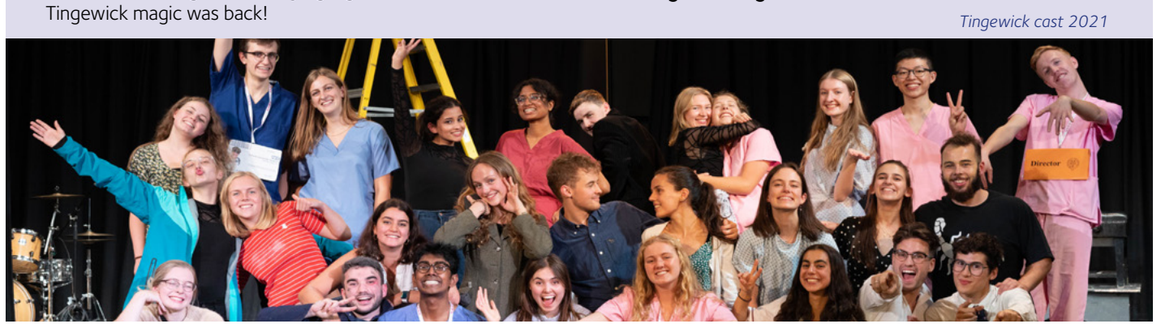
This year, we're raising money for Oxford Hospitals Charity and Calon Hearts; both of which mean a lot to us. We started with some online fundraisers, including quizzes, a virtual bake sale and the hugely successful Oxford Unlocked raffle. We've since been able to reintroduce more traditional Tingewick events such as the Ceilidh and the Consultant Gameshow. These were augmented by two huge physical endeavours: the Three Peaks Challenge and a 48-hour non-stop Headington Hill runathon. A highlight for many was our September production of 'Nightsweats at the Museum'. With Tingewick Hall off-limits, we took Tingeaid 2021 into St John's College where we sang and danced through one terrifying nightshift at the JR. The Tingewick magic was back!

We've already raised over £20,000, and that's before launching our biggest fundraiser of the year: the Tingewick Pantomime. Sadly, the pantomime couldn't happen last year - but elephants never forget, so we'll be back and (hopefully) better than ever! This year, we're honouring Tingewick's legacy by transporting you from the present day back to a pre-pandemic time with our production of 'Doctor Flu: The Shoe Must Go On'.

We've worked so hard to keep the spirit of Tingewick going and can't wait to see you all at the pantomime in January. We're taking Tingewick to an all-new venue in the Amey Theatre, Abingdon. The heart of Tingewick remains the same, and Rita will still be on hand to save the day! Despite the challenges of the last two years, Tingewick thrives. We've raised money for incredible charities and energised the medical students - that really is something to be proud of.

The Tingewick Pantomime takes place 12 to 15 January 2022 at the Amey Theatre in Abingdon. Tickets are on sale via **bit.ly/doctorflu**

www.tingewick.org



Tingewick cast 2021

Osler House Boat Club News

Jennifer Holmes
(2017 St Hugh's College), OHBC President

OHBC has had a busier term than ever, all culminating in our biggest challenge - an epic journey to row everyone's favourite pink elephant all the way to London!

September saw an influx of keen fourth years bringing fresh blood into the club and committee. More importantly, we now have a men's side desperate to show that it is not just the women of OHBC who can win blades.

Halloween brought IWL A, with our W2 8+ the fourth fastest women's boat of the day and the W1 4+ coming second in their category and beating half of the eights. Setting the tone for another speedy year from OHBC! October also saw another alumni outing - only in OHBC can you take out a boat of alumni on Sunday to end up in the JR ED with them the very next day! Do get in touch if you want to come down for a row; we enjoy getting back on the water with you.

Meanwhile, November saw OHBC partnering with your favourite pink elephant, rowing an eight 170km and through 33 locks from Oxford to London over three days. Around 20 members of OHBC took part in this challenge helping to raise £7,900 to date, meaning a £3,950 donation to Tingewick to help support the Oxford Hospitals Charity and Calon Hearts.

If this term has sounded busy just wait for 2022 which will hold more racing, more alumni events, and hopefully, even more bumps than last year! I am also happy to announce that you can now get your hands on an infamous OHBC Bucket hat - as seen in last year's bumps commentary.

We are all thankful for your continued support of the Club – we could not do this without you. To hear more and to receive invites to future events, remember to sign up to our mailing list by dropping us an email (oslerhousebc.president@gmail.com).

Best wishes from all of us at OHBC!

Gofundme: gf.me/u/zcf4kp
@oubc_oxford
@ohbc.oxford

Rita on the river

Alumni after fundraising Row, September 2021

OHBC crew after fundraising Row from Oxford to London

Covid-19 Art Competition Winner

Matthew Gowell
(2015 New College)

In my final week of medical school, I spent time documenting the experiences of staff who worked on the frontline during the first wave of the pandemic. During a visit to intensive care at the John Radcliffe, I photographed a poignant moment of embrace between Liza and Linda, a nurse and healthcare assistant. This was one of the few ways it was possible to physically comfort a colleague, whilst social distancing was enforced - dressed in full PPE. They told me that this practice became commonplace amongst the nursing staff and helped strengthen their resolve when they felt most affected by the harrowing events unfolding around them.

I instantly knew that I had to paint this image. It perfectly encapsulates the need for human interaction and its resilience during the most adverse of circumstances. I hope that this painting will serve as a lasting reminder of the strength of our NHS key workers and the sacrifices they made, during one of the most significant events of the twenty-first century unfolding.

‘Embrace’ - Oil on canvas, 1m x 1.2m

The Radcliffe Orchestra Returns

Professor John Stradling *Emeritus Professor of Respiratory Medicine, University of Oxford*

The Radcliffe Orchestra gave its first live concert, since government Covid-19 restrictions were lifted, on Saturday 06 November in aid of The Oxford Christmas Day Lunch. It was a joyous occasion to be making music together again in front of a live reactive audience. Paediatric registrar Shuang Wang and consultant anaesthetist Pete Hambly played Shostakovich’s 2nd piano concerto and Mozart’s 23rd piano concerto respectively, followed by Beethoven’s 1st symphony, all under the baton of one of our regular conductors, Andrew Gray. Ticket numbers were limited to 120, so our usual number of concert goers will have to wait until our 12 March concert.

The Radcliffe Orchestra started in 1978 when a group of hospital musicians, led by respiratory consultant Dr Donald Lane, gave a concert in memory of a young nurse, Jill Broadis, who had died of melanoma. A memorial fund for cancer research was launched in her name, helped by an annual concert for 20 years. The number of musicians grew to a full-size symphony orchestra. The players are made up of various health professionals, often with support from friends and family. The orchestra normally puts on three fundraising concerts a year, each raising about £1,000 for medically related charities. In 2016, it gave its 100th concert. The Oxford Radcliffe Hospitals Charitable Funds support the orchestra and regard it as an important social amenity within the Oxford Health Services.

How important is music in your life? (ed)

I had all but given up playing the trumpet as a busy junior doctor but my then boss, Donald Lane, asked me to play in one of his concerts having remembered my rather out-of-date entry on the CV! This resurrected my playing, and since then music has been a great source of sanity, counteracting the trials and tribulations of working in the NHS. Playing in an orchestra is an all-round wonderful experience on many different levels: the music itself; the camaraderie within the orchestra; and the satisfaction of playing as well as possible (and not letting down the rest of the orchestra!).

What happened to the Orchestra during Lockdown?

During lockdown, in the Summer of 2020, Catherine Underwood (who had been due to conduct the June 2020 concert) and her family organised an immensely successful online production of the orchestra playing Nimrod from Elgar’s Enigma Variations. This involved all of us individually recording our parts at home, and then the Underwood family, through extraordinary technical wizardry, combined all the recordings into a very professional production. This raised over £4,000 for the Oxford Hospitals Charity.

The recording can be found here: **www.hospitalcharity.co.uk/news/radcliffeorchestra**

As a respiratory physician, what did you think about the strict lockdown measures for musicians and choirs?

Lockdown was a disaster for music, both professional and amateur. We know of professional musicians who had to sell their house due to the catastrophic loss of income and no government support. Only now are we seeing the return of live concerts, albeit with various restrictions, and the obvious joy with which musicians are once again performing. Some of the restrictions have been in my view sensible, others over restrictive, particularly for choirs. There are going to be many amateur musical groups who will have lost the incentive to keep going.

Lockdown restrictions have done much harm, but you need the wisdom of Solomon to weigh up the chalk and cheese issues involved. One can argue very different viewpoints, given the limited evidence available, on many of the issues over transmissibility in different social activities such as singing and playing musical instruments. We will probably never know, even in retrospect, whether the UK got it right or not.

Looking forward...

George Caird will once again be conducting us for our next concert on 12 March, in aid of The Porch Day Centre. See **www.radcliffeorchestra.org.uk** for details.

Dr Rosie Adams, a breast radiologist at the Churchill, is the orchestra chairman. She can be contacted at **rosie.adams@ouh.nhs.uk** and would be delighted to hear from medically related charities who might like the Radcliffe Orchestra to do a concert for them, as well as any musicians interested in joining the orchestra.

Performance in St Michael and All Angels Church, Summertown, November 2021

Grow Your Own Woodland

Dr Fiona Hampton
(1974 St Hugh's College), Retired Consultant Pediatrician

The plan for my consultant job was always to live in the countryside and commute to a paediatric unit big enough for me to teach. It did not originally include growing our own small forest.

I did not know much about Middlesbrough or The North York Moors 25 years ago, but we have lived within the park boundaries, only eight miles from the hospital.

Our former farmworker's cottage is in the middle of what had been a large country house estate of agricultural land, largely hillside grazing, some of which had been planted with trees in the previous five years. We felt encouraged to do the same with our two hectares of land. A Forestry Commission grant covered half the cost of planting 2,500 mixed native broadleaves 15 months after we moved in. Seeing our green credentials, the owner of the surrounding land sold us an unplanted plot adjacent to ours and a year later, with the help of another grant, my GP husband Chris took leave to supervise planting 4,000 more trees assisted by a local youth opportunity scheme. The following year, we bought all his remaining land, mostly already planted, and finally, five years ago, we planted our last tree-free area. A drive to make wildlife corridors and encourage willow tits made us eligible for a new scheme to plant broadleaves with a preponderance of willow. This time we were assisted by mountain bikers whom we promised could build a track in return.

Trees need more work than you might expect as you see them on the hillside in their plastic tubes. Initially, they need surrounding vegetation to be cleared to allow them light and energy, in our case mostly bracken which is very difficult to control. There is a high death rate, with voles eating the roots, and the grants require deaths to be replaced. Later trees get blown over or pulled down by bracken or trespassing sheep and need re-staking. If short tubes are used, as the previous owner did, grazing roe deer remove the lead stem and one has to be identified before putting a taller tube on. The older tubes did not biodegrade as they should and strangled the trees, needing manually splitting.

Finally, after 20 years, the plantation needs thinning so stronger trees can thrive and to produce areas for different animal and plant species, along with new planting so trees are not of a uniform age. We have an approved plan for this and before Covid-19 we got together with a college to bring their students to cut down trees. We hope this will restart next year.

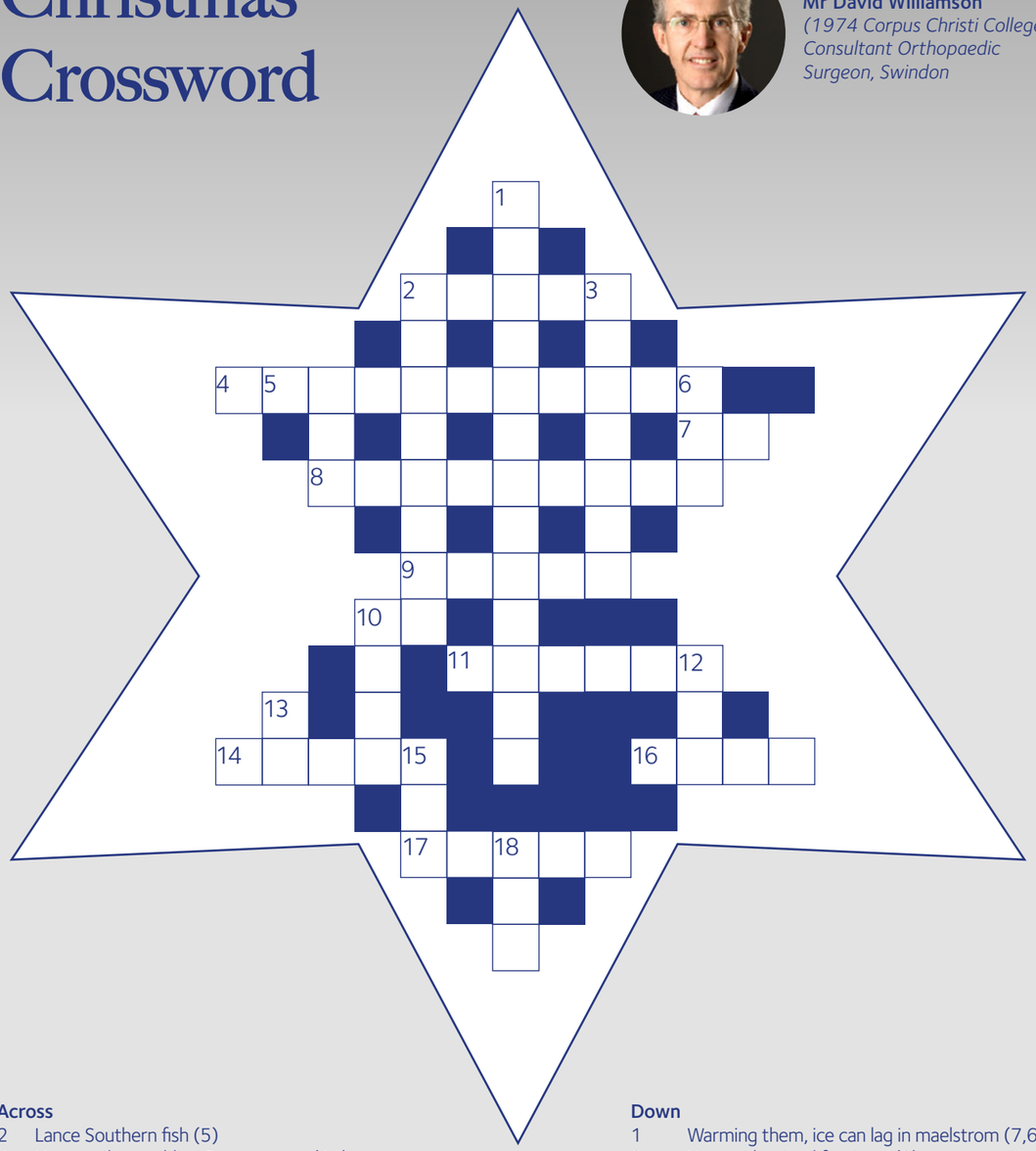
Working outside with the trees in all weathers has been a wonderful antidote to the stresses of NHS work. Being physically exhausted but emotionally relaxed is just what these doctors needed. I remember planting trees one snowy boxing day listening to Stephen Fry reading the whole of the first Harry Potter on Radio 4. Perfect.

Chris retired at 54 to spend more time on the land and bought himself a JCB. The first job with it was to install a 6kW wind turbine. I waited until 58 and bought an alpine tractor; good on hills. Working outside now ensures we keep fit. We have a small sawmill and lots of woodworking equipment so we can make furniture with wood from fallen trees and a biomass log boiler to heat the house with waste wood.

We are now proud owners of 36 hectares of hillside bearing about 30,000 young trees, as well as some areas of woodland over 100 years old. Of course, land is more affordable "up north" but you don't have to aspire to growing such a big wood as we have; every little helps but get a move on. They say the best time to plant a wood is 20 years ago, because after that you will have a canopy, and that's both cool and green.

Christmas Crossword

Mr David Williamson
(1974 Corpus Christi College), Consultant Orthopaedic Surgeon, Swindon



Across

2 Lance Southern fish (5)
4 Heat made trembling Peter mature (11)
7 Sounds like cattle in the Bible (2)
8 Arrange year after English sailor goes terrestrial (9)
9 Pigment found in Loch Restil (5)
10 No back and forth (2)
11 Future source of protein? Turning sin, etc (6)
14 Coiling a rope for a musical (5)
16 Underground pipe (4)
17 Sounds like the best spreadsheet (5)

Down

1 Warming them, ice can lag in maelstrom (7,6)
2 Note rash ruined furniture (8)
3 Teach editor and accountant in vehicle (7)
5 Backward girl finds her way? (3)
6 In lovely cathedral (3)
10 Headless dog at an end (4)
12 Thank you for Greek letter (3)
13 Lost quiet little dog at the top (2)
15 Top club? (3)
18 Police the conference (3)

Clues 16, 14 and 11 (in that order) give a **what3words** location. Where is this controversial location?

Solution on page 44

ANSWERS TO CROSSWORD

Across
2 Spike
4 Temperature
7 Lo
8 Planetary
9 Ochre
10 On
11 Insect
14 Opera
16 Tube
17 Excel

Down
1 Climate change
2 Sheraton
3 Educate
5 Map
6 Ely
10 Over
12 Tau
13 Up
15 Ace
18 Cop

The location: tube.opera.insect on what3words is in Linacre College.

Short-eared owl © **Dr John Reynolds** (1975 St Catherine's College), Associate Head of Medical Sciences Division (Clinical Affairs) and Consultant Physician and Clinical Pharmacologist, John Radcliffe Hospital, Oxford.

"I gravitate to the Otmoor RSPB reserve for a quiet hour. It is a remarkable place with an abundance of wildlife where I can indulge my hobby of wildlife photography".